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FILE 'HOME' ENTERED AT 15:36:37 ON 16 JAN 2003

=> file reg COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 15:36:53 ON 16 JAN 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 American Chemical Society (ACS)

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STRUCTURE FILE UPDATES: 15 JAN 2003 HIGHEST RN 479190-61-9 DICTIONARY FILE UPDATES: 15 JAN 2003 HIGHEST RN 479190-61-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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E4	3	AMINOISOPHTHALO/BI
E5	1	AMINOISOPHTHALONITRILE/BI
E6	2	AMINOISOPHTHALOYL/BI
E7	3	AMINOISOPR/BI
E8	3	AMINOISOPRENE/BI
E9	3	AMINOISOPROP/BI
E10	7	AMINOISOPROPAN/BI
E11	7	AMINOISOPROPANOL/BI
E12	3	AMINOISOPROPOXY/BI

=> s e1-e6

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- 1 AMINOISOPHTHALONITRILE/BI
- 2 AMINOISOPHTHALOYL/BI
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- => s e1-e11
- 8 AMINOISOPHTHALANILIDE/BI
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- 41 AMINOISOPHTHALIC/BI
- 3 AMINOISOPHTHALO/BI
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- 3 AMINOISOPRENE/BI
- 3 AMINOISOPROP/BI
- 7 AMINOISOPROPAN/BI
- 7 AMINOISOPROPANOL/BI
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- => e tridecanediamine

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E11	11	TRIDECANEDINITRILE/BI
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## => s e1-e11

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- => file caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 119.36 119.57

FILE 'CAPLUS' ENTERED AT 15:38:57 ON 16 JAN 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 16 Jan 2003 VOL 138 ISS 3 FILE LAST UPDATED: 15 Jan 2003 (20030115/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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(FILE 'HOME' ENTERED AT 15:36:37 ON 16 JAN 2003)

FILE 'REGISTRY' ENTERED AT 15:36:53 ON 16 JAN 2003

E AMINOISOPHTHALIC

L1 66 S E1-E6

L2 79 S E1-E11

E TRIDECANEDIAMINE

L3 133 S E1-E11

FILE 'CAPLUS' ENTERED AT 15:38:57 ON 16 JAN 2003

≈> s 12

L4 2431 L2

=> s 13

L5 439 L3

=> s 14 and 15

L6 2 L4 AND L5

=> d 16 1-2

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS

AN 2000:573551 CAPLUS

DN 133:164737

TI Elastomeric-modified phenolic rosin resins for pigment binders

IN Matzinger, Michael D.; Hutter, Frederick G.

PA Westvaco Corporation, USA

SO Eur. Pat. Appl., 6 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 2

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EP 1028131
                     A3 20001025
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
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                                         US 1999-248735
                     A 20001128
                                                           19990211
PRAI US 1999-248735
                      Α
                           19990211
    US 1998-61693
                      B2
                          19980416
    ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
L6
AN
    1983:81520 CAPLUS
    98:81520
DN
ΤI
    Tricyclic imidyl derivatives
ΙN
     Zweifel, Hans; Schilling, Walter; Storni, Angelo; Bellus, Daniel
PΑ
     Ciba-Geigy Corp. , USA
SO
    U.S., 13 pp. Cont.-in-part of U.S. 4,242,264.
     CODEN: USXXAM
DT
     Patent
LΑ
    English
FAN.CNT 2
    PATENT NO. KIND DATE
                                         APPLICATION NO.
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                                          ______
PΙ
    US 4337200
                    A 19820629
                                         US 1980-183905
                                                           19800904
                     Α
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                          19801230
                                         US 1979-9985
                                                           19790206
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                                         CA 1982-393611
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    US 4414394
                     A 19831108
                                        US 1982-349419
                                                           19820216
    US 4418200 A 19831129
US 4423231 A 19831227
US 4424366 A 19840103
US 4487942 A 19841211
US 4486596 A 19841204
CH 1978-1400
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    US 1982-349419
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    US 1982-349420
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    ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
    2000:573551 CAPLUS
AN
DN
    133:164737
TI
    Elastomeric-modified phenolic rosin resins for pigment binders
    Matzinger, Michael D.; Hutter, Frederick G.
    Westvaco Corporation, USA
    Eur. Pat. Appl., 6 pp.
    CODEN: EPXXDW
DT
    Patent
LA
    English
TC
    ICM C08G008-10
    ICS C08L061-06; C09D011-10
CC
    37-3 (Plastics Manufacture and Processing)
FAN.CNT 2
    PATENT NO.
                     KIND DATE
                                          APPLICATION NO. DATE
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    EP 1028131
                      A2
                           20000816
                                          EP 2000-400399 20000211
    EP 1028131
                     A3 20001025
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO
                    A 20001128
    US 6153693
                                         US 1999-248735
                                                           19990211
```

PRAI US 1999-248735 Α 19990211 US 1998-61693 В2 19980416 An improved method for producing pigment binder compns. comprises reacting in a condensation re- action: (a) 50-95% of a member selected from the group consisting of rosin esters, phenolic-modified rosin esters, reactive hydrocarbon resins, and combinations thereof; (b) 2-25% of a member selected from the group consisting of polyols contg. from 2 to 6 hydroxyl groups, amines contg. from 2 to 5 amine groups, alkanolamines contg. from 2 to 6 amine groups and/or hydroxyl groups, and combinations thereof, and (c) wherein the improvement comprises the addn. of 2-50% of the reactants of a member selected from the group consisting of butadiene homopolymers contg. at least one amine group, butadiene homopolymers contg. at least one carboxyl group, butadiene homopolymers contg. at least one hydroxyl group, butadiene homopolymers contg. at least one anhydride group, butadiene homopolymers contg. at least one epoxy group, and combinations thereof, to produce the pigment binder compn. In particular, the invention relates to elastomeric-modified pigment binder compns. which exhibit properties that make them useful in formulating vehicles for lithog. printing inks and other coating applications. phenolic resin elastomer modified pigment binder ST Binders IΤ Pigments, nonbiological (elastomeric-modified phenolic rosin resins for pigment binders) IT Phenolic resins, uses Polyoxyalkylenes, uses Tall oil rosin RL: TEM (Technical or engineered material use); USES (Uses) (elastomeric-modified phenolic rosin resins for pigment binders) ΙT Resin acids RL: TEM (Technical or engineered material use); USES (Uses) (esters; elastomeric-modified phenolic rosin resins for pigment binders) Butadiene rubber, uses IT RL: TEM (Technical or engineered material use); USES (Uses) (hydroxy-terminated; elastomeric-modified phenolic rosin resins for pigment binders) IT Inks (lithog.; elastomeric-modified phenolic rosin resins for pigment binders) ITButadiene rubber, uses RL: TEM (Technical or engineered material use); USES (Uses) (maleated; elastomeric-modified phenolic rosin resins for pigment binders) IT Hydrocarbons, uses RL: TEM (Technical or engineered material use); USES (Uses) (resins; elastomeric-modified phenolic rosin resins for pigment binders) IT 9003-17-2 RL: TEM (Technical or engineered material use); USES (Uses) (butadiene rubber, hydroxy-terminated; elastomeric-modified phenolic rosin resins for pigment binders) 9003-17-2 IT RL: TEM (Technical or engineered material use); USES (Uses) (butadiene rubber, maleated; elastomeric-modified phenolic rosin resins for pigment binders) 50-70-4, Sorbitol, uses ΙT 56-81-5, 1,2,3-Propanetriol, uses 1,2-Propanediol, uses 69-65-8, Mannitol 77-85-0 77-86-1, Tris(hydroxymethyl)aminomethane 77-99-6, Trimethylolpropane Tripentaerythritol 78-90-0, 1,2-Propylene diamine **78-96-6**, Isopropanolamine 80-05-7, uses 95-54-5, o-Phenylenediamine, uses 95-80-7 96-27-5, 1-Thioglycerol 101-77-9 102-71-6, uses 102-79-4, N-Butyldiethanolamine 104-10-9, 4-Aminophenethyl alcohol 105-08-8,

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1,4-Cyclohexanedimethanol 105-59-9 105-83-9
                                                        106-50-3,
     p-Phenylenediamine, uses 107-15-3, 1,2-Ethanediamine, uses
     1,2-Ethanediol, uses 107-88-0, 1,3-Butanediol 108-31-6, Maleic
     anhy-dride, uses 108-45-2, 1,3-Benzenediamine, uses 109-76-2,
     Trimethylenediamine 109-83-1, N-Methylethanolamine
                                                             110-60-1,
     Tetramethylene diamine 110-63-4, 1,4-Butanediol, uses 110-85-0,
     Piperazine, uses 110-97-4, Diisopropanolamine 111-29-5, 1,5-Pentanediol 111-40-0, Diethylene triamine 111-41-1
                                                                   111-42-2,
           111-46-6, uses 112-24-3 112-27-6 112-57-2, Tetraethylene
                115-69-5, 2-Amino-2-methyl-1,3-propanediol 115-70-8,
     pentamine
     2-Amino-2-ethyl-1,3-propanediol 115-77-5, uses 120-07-0 122-20-3, Triisopropanolamine 124-09-4, 1,6-Hexanediamine, uses 126-30-7
     126-58-9, Dipentaerythritol 139-87-7, N-Ethyldiethanolamine 141-43-5,
     uses 143-23-7, Bis(hexamethylene) triamine 156-87-6,
                          479-27-6, 1,8-Diaminonaphthalene
                                                             502-32-9, Leucinol
     3-Amino-1-propanol
     504-63-2, 1,3-Propanediol 584-03-2, 1,2-Butanediol 589-37-7,
     1,3-Pentanediamine 616-30-8, 3-Amino-1,2-propane-diol 623-04-1,
     4-Aminobenzyl alcohol 629-11-8, 1,6-Hexanediol 694-83-7,
     1,2-Diaminocyclohexane 823-40-5, 2,6,-Tolylenediamine
     2-(2-Aminoethoxy)ethanol
                                1761-71-3, Bis (4-aminocyclohexyl) methane
     1877-77-6, 3-Aminobenzyl alcohol 2508-29-4, 5-Amino-1-pentanol
     3114-70-3, 1,4-Diaminocyclohexane 3306-06-7, 2-Amino-1-phenyl-1,3-
     propanediol 3385-21-5, 1,3-Diaminocyclohex-ane 4067-16-7,
     Pentaethylenehexam-ine 4097-89-6, Tris(aminoethyl)amine 4253-76-3,
     N-Stearyl trimethylene diamine 4379-13-9, Isoleucinol
                                                                4426-48-6,
     1,2-Butylene diamine 4985-85-7, N-(3-Aminopropyl) dieth-anolamine
     5339-85-5, 2-Aminophenethyl alcohol 6850-38-0, 2-Aminocyclohexanol
     6850-39-1, 3-Aminocyclohexanol
                                     6850-65-3, 4-Amino-cyclohexanol
     7173-62-8, N-Oleyl trimethylene diamine 7568-93-6, 2-Amino-1-
     phenylethanol 9003-17-2D, Butadiene homopolymer, functional group-contg.
     15520-10-2
                 16369-05-4, 2-Amino-3-methyl-1-butanol 16369-14-5,
     2-Amino-1-pentanol
                         16397-19-6, 2-Amino-1-hexanol
                                                           23235-61-2,
     Ditrimethylolpropane 24800-44-0, Tripropylene glycol 25119-62-4,
     Styrene-allyl alcohol copolymer 25154-52-3, Nonylphenol 25265-71-8, Dipropylene glycol 25322-68-3 28631-79-0, Aminoethylpiperazine
     30525-89-4, Paraformaldehyde 45007-61-2, Hexitol
                                                         48115-38-4,
     .alpha.-(1-Aminoethyl) benzyl alcohol 68148-42-5, Glycerol
     monothioglycolate
     RL: TEM (Technical or engineered material use); USES (Uses)
        (elastomeric-modified phenolic rosin resins for pigment binders)
    ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
     1983:81520 CAPLUS
     98:81520
     Tricyclic imidyl derivatives
     Zweifel, Hans; Schilling, Walter; Storni, Angelo; Bellus, Daniel
     Ciba-Geigy Corp. , USA
     U.S., 13 pp. Cont.-in-part of U.S. 4,242,264.
     CODEN: USXXAM
     Patent
     English
     C07D209-90; C07D209-94
NCL
    548451000
     74-5 (Radiation Chemistry, Photochemistry, and Photographic and Other
     Reprographic Processes)
FAN.CNT 2
    PATENT NO.
                     KIND DATE
                                           APPLICATION NO. DATE
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    US 4337200 A 19820629
                                          US 1980-183905 19800904
    US 4242264
                     A 19801230
                                          US 1979-9985 19790206
    CA 1138468 A2 19821228
US 4414394 A 19831108
                                          CA 1982-393611 19820105
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US 1982-349419 19820216

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    US 4418199
                       Α
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    US 1980-183905
                            19800904
    US 1982-349419
                            19820216
     US 1982-349420
                            19820216
GΙ
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Ι

AB A photocrosslinkable polymer suitable for prepn. of the printing plates for offset printing and as photoresists is prepd. with a tricyclic imidyl deriv. I (Z = C1-30 alkylene, C5-6 cycloalkylene, methylenebis(cyclohexylene), C6-10 arylene, C7-8 aralkylene, C7-8 alkylarylene or arylene substituted by C1-4 alkyl, C1-4 alkoxy or NO2; R = NH2, NH, C1-4 alkyl; R1,R2 = H, halogen, C1-4 alkyl or methoxy). Thus, an Al sheet support was coated with a 5% DMF soln. of a photocrosslinkable polymer obtained by copolymn. of maleic anhydride-Me vinyl ether copolymer and N-(2'-hydroxyethyl)-3,4-dihydronaphthalene-1,2-dicarboximide, dried, imagewise exposed by a 400 W Hg lamp at 40 cm distance for 6 min, and developed 3 s in THF and 30 s in 3% NaHCO3.H2O to give an image corresponding to 9 steps in a step wedge.

ST photopolymer tricyclic imidyl deriv photoresist; lithog plate photopolymer tricyclic imidyl

IT Lithographic plates

(offset, photopolymers for fabrication of, prepn. of, from tricyclic imidyl derivs.)

IT Resists

(photo-, for prepn. of photopolymers for photoresists and lithog. printing plates)

IT 72198-39-1 72198-42-6 72198-43-7 72198-46-0 72198-47-1 72198-48-2 72198-49-3 72198-50-6 72198-51-7 72198-52-8 72198-53-9 72198-54-0 72199-03-2 73005-41-1 73005-42-2 83591-34-8 83591-35-9

RL: USES (Uses)

(for prepn. of photopolymers for photoresists and lithog. plates)
IT 60-32-2 141-43-5, uses and miscellaneous 14438-56-3 26734-09-8
37845-14-0 62351-76-2 72198-40-4 72198-44-8 73005-43-3
74926-27-5

RL: USES (Uses)

(for prepn. of photopolymers for photoresists and lithog. printing plates)

IT 9011-16-9D, reaction products with (aminoethyl)dihydronaphthalenedicarboxi mide 72199-04-3 72199-05-4 72231-41-5 72231-42-6 72231-43-7 72231-44-8 83592-37-4

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RL: USES (Uses)
        (photoimaging compn. contg., prepn. of)
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     72231-39-1P
                   72231-40-4P
     RL: PREP (Preparation)
        (prepn. of, for photoresist and lithog. plate fabrication)
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E2
             1
                   EXTRACOPORAL/BI
E3
            18 --> EXTRACOPOREAL/BI
E4
             1
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E5
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E6
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E7
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E8
            1
                   EXTRACORDAL/BI
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E11
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=> d his (FILE 'HOME' ENTERED AT 15:36:37 ON 16 JAN 2003) FILE 'REGISTRY' ENTERED AT 15:36:53 ON 16 JAN 2003 E AMINOISOPHTHALIC L166 S E1-E6 L2 79 S E1-E11 E TRIDECANEDIAMINE L3 133 S E1-E11 FILE 'CAPLUS' ENTERED AT 15:38:57 ON 16 JAN 2003 L42431 S L2 L5 439 S L3 L6 2 S L4 AND L5 E EXTRACOPOREAL E EXTRACOPOREAL E EXTRACORPOREAL ь7 5405 S E1-E11 => s 14 and 17 4 L4 AND L7 L8=> d 18 1-4 L8 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS 2002:523951 CAPLUS ANDN 137:228855 ΤI Trifunctional conjugation reagents. Reagents that contain a biotin and a radiometal chelation moiety for application to extracorporeal affinity adsorption of radiolabeled antibodies ΑU Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.; Nilsson, Rune; Sandberg, Bengt E. B.; Brechbiel, Martin CS Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA Bioconjugate Chemistry (2002), 13(5), 1079-1092 SO CODEN: BCCHES; ISSN: 1043-1802 PB American Chemical Society DTJournal LA English RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT rsANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS ΑN 2001:923565 CAPLUS DN 136:42919 TIBiotin derivatives for an extracorporeal device ΙN Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune PA Mitra Medical Technology AB, Swed.; University of Washington SO PCT Int. Appl., 45 pp. CODEN: PIXXD2 DTPatent LΑ English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE \_ -- ------PΙ WO 2001095857 A2 20011220 WO 2001-SE1374 20010618

WO 2001095857

A3

20020328

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ΑN
     2000:35037 CAPLUS
DN
     132:90367
TI
     Trifunctional reagent for conjugation to a biomolecule for use in
     diagnosis and therapy
     Wilbur, D. Scott; Sandberg, Bengt E. B.
IN
PA
     Dept. of Radiation Oncology, University of Washington, USA; Mitra Medical
     Technology AB
SO
     PCT Int. Appl., 48 pp.
     CODEN: PIXXD2
DT
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LΑ
     English
FAN.CNT 2
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     WO 2000002051 A1 20000113
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ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
rs
AN
     2000:35036 CAPLUS
DN
     132:90366
TI
     Trifunctional reagent for conjugation to a biomolecule for use in
     diagnosis and therapy
    Wilbur, D. Scott; Sandberg, Bengt E. B.
IN
     Department of Radiation Oncology, University of Washington, USA; Mitra
PA
    Medical Technology AB
     PCT Int. Appl., 41 pp.
SO
    CODEN: PIXXD2
DT
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LA
     English
FAN.CNT 2
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    JP 2002519440
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L3
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L7
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L8
=> s 15 and 17
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ANSWER 1 CAPLUS COPYRIGHT 2003 ACS
     130:267698 CAPLUS
AN
     Synthesis of achiral linker reagents for direct labeling of
TI
     oligonucleotides on solid supports
ΑU
     Behrens, Carsten; Dahl, Otto
CS
     Department of Chemistry, University of Copenhagen, Copenhagen, DK-2100,
SO
     Nucleosides & Nucleotides (1999), 18(2), 291-305
     CODEN: NUNUD5; ISSN: 0732-8311
PB
     Marcel Dekker, Inc.
DT
     Journal
LΑ
     English
CC
     33-10 (Carbohydrates)
     Section cross-reference(s): 9
     Full exptl. procedures for the synthesis of a series of new functional
AB
     linker reagents and solid supports are reported. The achiral linker
     reagents and supports can be used for high yield incorporation of free
     amino groups, fluorescein or biotin into DNA oligomers.
     achiral amino linker oligonucleotide solidphase prepn fluorescent label;
     hybridization oligonucleotide achiral amino linker
ΙT
     Solid phase synthesis
        (of oligonucleotides contg. achiral amino linker reagents for direct
        labeling)
IT
     Nucleic acid hybridization
        (of oligonucleotides contg. achiral amino linker units)
TΤ
     Fluorescent substances
        (prepn. of using achiral amino linker reagents for direct labeling of
        oligonucleotides)
ΙT
     Oligonucleotides
     RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP
     (Preparation); RACT (Reactant or reagent)
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        oligonucleotides on solid supports)
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     solid-supported
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                       221318-06-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of in the synthesis of achiral amino linker
        reagents for direct labeling of oligonucleotides on solid supports)
IT
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                   171717-19-4P 171717-20-7P
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     171844-08-9P
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     188366-86-1P
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                                                  188420-43-1P
                                                                  188420-44-2P
     222054-01-5P
                   222054-02-6P
                                   222054-03-7P
                                                  222054-04-8P
                                                                  222054-05-9P
    RL: SPN (Synthetic preparation); PREP (Preparation)
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(prepn. of using achiral amino linker reagents for direct labeling of oligonucleotides on solid supports)

IT 221889-90-3P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. of using achiral amino linker reagents in one chain and effect on hybridization)

IT 221889-92-5P 221889-94-7P 221889-96-9P 221889-98-1P 221890-00-2P RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of using achiral amino linker reagents in one chain and effect on hybridization)

IT 618-88-2 3282-30-2, Pivaloyl chloride 3326-32-7 28920-43-6,

9-Fluorenylmethyl chloroformate 35013-72-0 RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of in the synthesis of achiral amino linker reagents for direct labeling of oligonucleotides on solid supports)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

- (1) Bannwarth, W; Helv Chim Acta 1987, V70, P175 CAPLUS
- (2) Beaucage, S; Protocols for Oligonucleotide Conjugates Synthesis and Analytical Techniques 1994
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- (6) Nelson, P; Nucleic Acid Res 1992, V20, P6253 CAPLUS
- (7) Perich, J; Tetrahedron Lett 1987, V28, P101 CAPLUS
- (8) Smith, L; Nucleic Acid Res 1985, V13, P2399 CAPLUS
- (9) Tarrason, G; Antisense Research and Development 1995, V5, P193 CAPLUS
- (10) Wachter, L; Nucleic Acid Res 1986, V14, P7985 CAPLUS

## => d 126:207193 all

#### ANSWER 1 CAPLUS COPYRIGHT 2003 ACS

- AN 126:207193 CAPLUS
- TI Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin Ring Carboxylates and Evaluation of Their Binding to Transcobalamin. 2
- AU Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon; Quadros, Edward V.; McLoughlin, Patricia; Morgan, A. Charles
- CS Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
- SO Bioconjugate Chemistry (1997), 8(2), 161-172 CODEN: BCCHES; ISSN: 1043-1802
- PB American Chemical Society
- DT Journal
- LA English
- CC 1-6 (Pharmacology)
  - Section cross-reference(s): 78
- AΒ Several cobalamin (Cbl) dimers have been prepd. for evaluation as potential antiproliferative agents in the treatment of AIDS-related lymphoma. The Cbl dimers were synthesized by crosslinking Cbl carboxylates, produced by acid hydrolysis of the b-, d-, and e-propionamide side chains of cyanocobalamin (CN-Cbl), through an isophthalate mol. Linking mols. were used between the Cbl carboxylates and the isophthalate moiety. The linkers were incorporated to provide a distance between the two Cbl mols. such that the dimeric Cbls might bind two mols. of transcobalamin II (TCII), the Cbl transport protein in plasma. Initially, the linking moiety used was 1,12-diaminododecane, but the resulting dimers had low aq. soly. To improve the soly. of the dimers, 4,7,10-trioxa-1,13-tridecanediamine was employed as the linking moiety. This improved the water soly. of the dimers considerably, while retaining the distance between the Cbl mols. at 41-42 .ANG. (fully extended). To introduce addnl. substitution on Cbl dimers,

```
5-aminoisophthalic acid was used as the crosslinking reagent.
     P-Iodobenzoyl and p-(tri-n-butylstannyl)benzoyl conjugates of
     5-aminoisophthalate were synthesized and used to prep. Cbl dimers.
     stannylbenzoyl-conjugated Cbl dimers were prepd. as precursors to be used
     in radioiodination reactions, and the iodobenzoyl-conjugated Cbl dimers
     were prepd. as HPLC stds. for the radioiodinated product. Attempts to
     iodinate/radioiodinate the stannylbenzoyl Cbl dimers were unsuccessful.
     Although an explanation for this is not readily apparent, the failure to
     react may be due to the lipophilicity of the linker used and the steric
     environment of the two Cbl moieties. A biotinylated deriv. of
     5-aminoisophthalate was also synthesized and used to prep.
     biotinylated-Cbl dimers. In a competitive rhTCII binding assay with
     [57Co]CN-Cbl, Cbl dimers contg. the lipophilic diaminododecane linking
     moiety had decreased binding avidities compared to those of Cbl monomers
     substituted at the same corrin ring carboxylate. However, Cbl dimers
     contg. the water-solubilizing trioxadiamine linker appeared to have
     avidities similar to those of the Cbl monomers.
     cobalamin dimer prepn transcobalamin binding
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     study, unclassified); SPN (Synthetic preparation); BIOL (Biological
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        (prepn. of cobalamin dimers and binding to human recombinant
        transcobalamin II)
     12651-28-4, Transcobalamin II
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (prepn. of cobalamin dimers and binding to human recombinant
        transcobalamin II)
     68-19-9P, Cyanocobalamin
     RL: PUR (Purification or recovery); PREP (Preparation)
        (prepn. of cobalamin dimers and binding to human recombinant
        transcobalamin II)
     58-85-5P, Biotin
                                   26264-28-8P
                        99-31-0P
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     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
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        (prepn. of cobalamin dimers and binding to human recombinant
        transcobalamin II)
=> d 126:3868 ALL
ANSWER 1 CAPLUS COPYRIGHT 2003 ACS
     126:3868 CAPLUS
     Antibody Fragments in Tumor Pretargeting. Evaluation of Biotinylated Fab'
     Colocalization with Recombinant Streptavidin and Avidin
     Wilbur, D. Scott; Hamlin, Donald K.; Vessella, Robert L.; Stray, James E.;
     Buhler, Kent R.; Stayton, Patrick S.; Klumb, Lisa A.; Pathare, Pradip M.;
     Weerawarna, S. Ananda
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
     Bioconjugate Chemistry (1996), 7(6), 689-702
    CODEN: BCCHES; ISSN: 1043-1802
    American Chemical Society
    Journal
    English
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ΑU

CS

SO

PB

DT

LA

CC

8-9 (Radiation Biochemistry)

Section cross-reference(s): 14 An evaluation of the use of a biotinylated monoclonal antibody Fab' ΑB fragment in tumor pretargeting was conducted. As a model system, tumor colocalization of avidin or recombinant streptavidin (r-streptavidin) and the biotinylated Fab' fragment (Fab'-S-biotin) of A6H, an antirenal cell carcinoma antibody, was evaluated in athymic mice bearing human renal cell carcinoma xenografts. A new water sol. sulfhydryl reactive biotinylation reagent, N-(13-N-maleimido-4,7,10-trioxatridecanyl)biotinamide, was synthesized and used for biotinylation of Fab'. A biodistribution of ChT-labeled A6H Fab'-S-biotin was conducted. Data from that distribution indicated that the Fab'-S-biotin localized well (i.e. 28% ID/g at 24 h) to human tumor xenografts in athymic mice. Subsequently, a biodistribution study involving pretargeting radioiodinated A6H Fab'-S-biotin to tumor xenografts, followed by administration of r-streptavidin at 4 or 20 h, was conducted. Specific colocalization of r-streptavidin to tumors contg. the A6H Fab'-S-biotin was evident from the data obtained. In a similar biodistribution study, specific colocalization of avidin to tumors pretargeted with A6H Fab'-S-biotin was also obsd. The avidin used in the study was radioiodinated with the N-hydroxysuccinimidyl ester of p-[1251]iodobenzoate ([1251]PIB-NHS). Very low concns. (e.g. 0.35% ID/q) of avidin colocalized at the tumor. To further show that specific colocalization within the tumor xenografts had occurred with biotinylated A6H Fab', radioiodinated avidin and r-streptavidin were co-injected into athymic mice bearing tumor xenografts to obtain their distributions without having biotinylated Fab' present. At 20 h postinjection, only small differences in the blood and tumor concns. of either protein were obsd., indicating that the specific tumor colocalization seen in the previous two biodistributions must have been due to the presence of Fab'-S-biotin. Calcns. were conducted to est. how much r-streptavidin (as a molar ratio) was colocalized. From the data obtained it was estd. that 36-61% of the tumor-localized Fab'-S-biotin mols. were bound with r-streptavidin and 4-23% bound with avidin, under the conditions studied. ST tumor pretargeting biotinylated monoclonal antibody ΙT Antibodies RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (monoclonal, Fab', biotinylated; renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin) TΤ RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin) ΙT Kidney, neoplasm (renal cell carcinoma; renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin) IT 173341-32-7P 183896-00-6P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate; renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin) ΙT 4246-51-9, 4,7,10-Trioxa-1,13-tridecanediamine 55750-48-6, N-Methoxycarbonylmaleimide 142685-25-4 RL: RCT (Reactant); RACT (Reactant or reagent) (reactant; renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin) ΙT 9013-20-1, Streptavidin RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

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(Uses)
        (renal cell carcinoma pretargeting using biotinylated Fab' monoclonal
        antibody with recombinant streptavidin and avidin)
ΙT
     58-85-5, Biotin
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (renal cell carcinoma pretargeting using biotinylated Fab' monoclonal
        antibody with recombinant streptavidin and avidin)
     183896-02-8P
ΙT
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (renal cell carcinoma pretargeting using biotinylated Fab' monoclonal
        antibody with recombinant streptavidin and avidin)
=> D 127:12587 ALL
ANSWER 1 CAPLUS COPYRIGHT 2003 ACS
     127:12587 CAPLUS
     Application of laser to the pretreatment of glass carbon electrode
TI
     Liu, Bin; Jinrui, Xu; Huang, Mialiang; Lin, Jianming
ΑU
     Dept. Applied Chemistry, Huagiao Univ., Quanzhou, 362011, Peop. Rep. China
CS
SO
     Huaqiao Daxue Xuebao, Ziran Kexueban (1996), 17(4), 362-364
     CODEN: HDZIEF; ISSN: 1000-5013
PB
     Huaqiao Daxue
DT
     Journal
LΑ
     Chinese
CC
     79-2 (Inorganic Analytical Chemistry)
     Section cross-reference(s): 72, 73
     The C electrodes for electroanal. were treated with laser. The effect of
AΒ
     pulse width, pulse energy, and irradn. time of laser on the preconcn. of
     Pb2+ in aq. (NH4)2SO4 and the anodic striping currents was studied. The
     stability, sensitivity, and reproducibility of C electrode were improved
     when the electrode was treated with a laser beam of 514.5 nm and a pulse
     width 25 ms for 2 min.
     carbon electrode laser treatment electrochem analysis
ΙT
     Electrodes
     Lasers
     Voltammetry
        (laser pretreatment of glass carbon electrode)
     7439-92-1, Lead, analysis
ΤТ
     RL: ANT (Analyte); ANST (Analytical study)
        (laser pretreatment of glass carbon electrode)
TΤ
     7440-44-0, Carbon, uses
     RL: DEV (Device component use); USES (Uses)
        (laser pretreatment of glass carbon electrode)
=> D HIS
     (FILE 'HOME' ENTERED AT 15:36:37 ON 16 JAN 2003)
     FILE 'REGISTRY' ENTERED AT 15:36:53 ON 16 JAN 2003
                E AMINOISOPHTHALIC
L1
             66 S E1-E6
L2
             79 S E1-E11
                E TRIDECANEDIAMINE
L3
            133 S E1-E11
     FILE 'CAPLUS' ENTERED AT 15:38:57 ON 16 JAN 2003
L4
           2431 S L2
L5
            439 S L3
L6
              2 S L4 AND L5
                E EXTRACOPOREAL
```

E EXTRACOPOREAL

E EXTRACORPOREAL

L7 5405 S E1-E11

L8 4 S L4 AND L7

L9 0 S L5 AND L7

=>

---Logging off of STN---

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	$\mathtt{TOTAL}$
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-3.91	-3.91

STN INTERNATIONAL LOGOFF AT 15:54:06 ON 16 JAN 2003

```
130:267698 CAPLUS
AN
     Synthesis of achiral linker reagents for direct labeling of
ΤI
     oligonucleotides on solid supports
ΑU
     Behrens, Carsten; Dahl, Otto
     Department of Chemistry, University of Copenhagen, Copenhagen, DK-2100,
CS
     Den.
     Nucleosides & Nucleotides (1999), 18(2), 291-305
SO
     CODEN: NUNUD5; ISSN: 0732-8311
     Marcel Dekker, Inc.
PB
DT
     Journal
LA
     English
     33-10 (Carbohydrates)
     Section cross-reference(s): 9
AB
     Full exptl. procedures for the synthesis of a series of new functional
     linker reagents and solid supports are reported. The achiral linker
     reagents and supports can be used for high yield incorporation of free
     amino groups, fluorescein or biotin into DNA oligomers.
ST
     achiral amino linker oligonucleotide solidphase prepn fluorescent label;
     hybridization oligonucleotide achiral amino linker
IT
     Solid phase synthesis
        (of oligonucleotides contg. achiral amino linker reagents for direct
        labeling)
IT
     Nucleic acid hybridization
        (of oligonucleotides contg. achiral amino linker units)
     Fluorescent substances
TT
        (prepn. of using achiral amino linker reagents for direct labeling of
      · oligonucleotides)
IT
     Oligonucleotides
     RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP
     (Preparation); RACT (Reactant or reagent)
        (synthesis of achiral amino linker reagents for direct labeling of
        oligonucleotides on solid supports)
ΙT
     99-31-0P
               42122-73-6P
                             71176-54-0P
                                            146335-23-1P
                                                           147190-36-1P
                                  171082-08-9DP, solid-supported
     171082-06-7P
                   171082-07-8P
     171082-09-0P
                  188257-47-8P
                                   188257-52-5P 188257-53-6DP,
     solid-supported
                       188257-54-7P
                                      188257-55-8P
                                                     188257-56-9DP,
     solid-supported
                       221318-06-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of in the synthesis of achiral amino linker
        reagents for direct labeling of oligonucleotides on solid supports)
                    171717-19-4P 171717-20-7P 171717-21-8P
IT
     171717-18-3P
                                                                 171717-22-9P
     171844-08-9P
                    188366-81-6P 188366-82-7P
                                                  188366-83-8P
                                                                 188366-85-0P
     188366-86-1P
                    188420-41-9P
                                   188420-42-0P
                                                  188420-43-1P
                                                                 188420-44-2P
     222054-01-5P
                    222054-02-6P
                                   222054-03-7P
                                                  222054-04-8P
                                                                 222054-05-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of using achiral amino linker reagents for direct labeling of
        oligonucleotides on solid supports)
IT
     221889-90-3P
     RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of using achiral amino linker reagents in one chain and effect
        on hybridization)
ΙT
     221889-92-5P
                                                  221889-98-1P
                   221889-94-7P
                                   221889-96-9P
                                                                 221890-00-2P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of using achiral amino linker reagents in one chain and effect
        on hybridization)
IT
     618-88-2
                3282-30-2, Pivaloyl chloride
                                               3326-32-7
                                                           28920-43-6.
     9-Fluorenylmethyl chloroformate 35013-72-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of in the synthesis of achiral amino linker reagents for
        direct labeling of oligonucleotides on solid supports)
RE.CNT 10
             THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
```

RE

- (1) Bannwarth, W; Helv Chim Acta 1987, V70, P175 CAPLUS
- (2) Beaucage, S; Protocols for Oligonucleotide Conjugates Synthesis and Analytical Techniques 1994
- (3) Beaucage, S; Tetrahedron 1993, V49, P1925 CAPLUS
- (4) Behrens, C; Bioorg Med Chem Lett 1995, V5, P1785 CAPLUS
- (5) Chu, B; DNA 1985, V4, P327 CAPLUS
- (6) Nelson, P; Nucleic Acid Res 1992, V20, P6253 CAPLUS (7) Perich, J; Tetrahedron Lett 1987, V28, P101 CAPLUS (8) Smith, L; Nucleic Acid Res 1985, V13, P2399 CAPLUS

- (9) Tarrason, G; Antisense Research and Development 1995, V5, P193 CAPLUS
- (10) Wachter, L; Nucleic Acid Res 1986, V14, P7985 CAPLUS

- AN 126:3868 CAPLUS
- TI Antibody Fragments in Tumor Pretargeting. Evaluation of Biotinylated Fab' Colocalization with Recombinant Streptavidin and Avidin
- AU Wilbur, D. Scott; Hamlin, Donald K.; Vessella, Robert L.; Stray, James E.; Buhler, Kent R.; Stayton, Patrick S.; Klumb, Lisa A.; Pathare, Pradip M.; Weerawarna, S. Ananda
- CS Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
- SO Bioconjugate Chemistry (1996), 7(6), 689-702 CODEN: BCCHES; ISSN: 1043-1802
- PB American Chemical Society
- DT Journal
- LA English
- CC 8-9 (Radiation Biochemistry) Section cross-reference(s): 14
- ΑB An evaluation of the use of a biotinylated monoclonal antibody Fab' fragment in tumor pretargeting was conducted. As a model system, tumor colocalization of avidin or recombinant streptavidin (r-streptavidin) and the biotinylated Fab' fragment (Fab'-S-biotin) of A6H, an antirenal cell carcinoma antibody, was evaluated in athymic mice bearing human renal cell carcinoma xenografts. A new water sol. sulfhydryl reactive biotinylation reagent, N-(13-N-maleimido-4,7,10-trioxatridecanyl)biotinamide, was synthesized and used for biotinylation of Fab'. A biodistribution of ChT-labeled A6H Fab'-S-biotin was conducted. Data from that distribution indicated that the Fab'-S-biotin localized well (i.e. 28% ID/g at 24 h) to human tumor xenografts in athymic mice. Subsequently, a biodistribution study involving pretargeting radioiodinated A6H Fab'-S-biotin to tumor xenografts, followed by administration of r-streptavidin at 4 or 20 h, was conducted. Specific colocalization of r-streptavidin to tumors contg. the A6H Fab'-S-biotin was evident from the data obtained. In a similar biodistribution study, specific colocalization of avidin to tumors pretargeted with A6H Fab'-S-biotin was also obsd. The avidin used in the study was radioiodinated with the N-hydroxysuccinimidyl ester of p-[1251]iodobenzoate ([1251]PIB-NHS). Very low concns. (e.g. 0.35% ID/g) of avidin colocalized at the tumor. To further show that specific colocalization within the tumor xenografts had occurred with biotinylated A6H Fab', radioiodinated avidin and r-streptavidin were co-injected into athymic mice bearing tumor xenografts to obtain their distributions without having biotinylated Fab' present. At 20 h postinjection, only small differences in the blood and tumor concns. of either protein were obsd., indicating that the specific tumor colocalization seen in the previous two biodistributions must have been due to the presence of Fab'-S-biotin. Calcns. were conducted to est. how much r-streptavidin (as a molar ratio) was colocalized. From the data obtained it was estd. that 36-61% of the tumor-localized Fab'-S-biotin mols. were bound with r-streptavidin and 4-23% bound with avidin, under the conditions studied.
- ST tumor pretargeting biotinylated monoclonal antibody
- IT Antibodies

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (monoclonal, Fab', biotinylated; renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin)

IT Avidins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin)

IT Kidney, neoplasm

(renal cell carcinoma; renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and

ΙT

avidin)

173341-32-7P 183896-00-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin)

IT 4246-51-9, 4,7,10-Trioxa-1,13-tridecanediamine 55750-48-6,

N-Methoxycarbonylmaleimide 142685-25-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(reactant; renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin)

IT9013-20-1, Streptavidin

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin)

IT 58-85-5, Biotin

RL: RCT (Reactant); RACT (Reactant or reagent)

(renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin)

ΙT 183896-02-8P

> RL: SPN (Synthetic preparation); PREP (Preparation) (renal cell carcinoma pretargeting using biotinylated Fab' monoclonal antibody with recombinant streptavidin and avidin)

126:207193 CAPLUS AN Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin Ring Carboxylates and Evaluation of Their Binding to Transcobalamin. 2 ΑU Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon; Quadros, Edward V.; McLoughlin, Patricia; Morgan, A. Charles CS Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA Bioconjugate Chemistry (1997), 8(2), 161-172 SO CODEN: BCCHES; ISSN: 1043-1802 PB American Chemical Society DTJournal LΑ English CC 1-6 (Pharmacology) Section cross-reference(s): 78 AΒ Several cobalamin (Cbl) dimers have been prepd. for evaluation as potential antiproliferative agents in the treatment of AIDS-related lymphoma. The Cbl dimers were synthesized by crosslinking Cbl carboxylates, produced by acid hydrolysis of the b-, d-, and e-propionamide side chains of cyanocobalamin (CN-Cbl), through an isophthalate mol. Linking mols. were used between the Cbl carboxylates and the isophthalate moiety. The linkers were incorporated to provide a distance between the two Cbl mols. such that the dimeric Cbls might bind two mols. of transcobalamin II (TCII), the Cbl transport protein in plasma. Initially, the linking moiety used was 1,12-diaminododecane, but the resulting dimers had low aq. soly. To improve the soly. of the dimers, 4,7,10-trioxa-1,13-tridecanediamine was employed as the linking moiety. This improved the water soly. of the dimers considerably, while retaining the distance between the Cbl mols. at 41-42 .ANG. (fully extended). To introduce addnl. substitution on Cbl dimers, 5-aminoisophthalic acid was used as the crosslinking reagent. P-Iodobenzoyl and p-(tri-n-butylstannyl)benzoyl conjugates of 5-aminoisophthalate were synthesized and used to prep. Cbl dimers. The stannylbenzoyl-conjugated Cbl dimers were prepd. as precursors to be used in radioiodination reactions, and the iodobenzoyl-conjugated Cbl dimers were prepd. as HPLC stds. for the radioiodinated product. Attempts to iodinate/radioiodinate the stannylbenzoyl Cbl dimers were unsuccessful. Although an explanation for this is not readily apparent, the failure to react may be due to the lipophilicity of the linker used and the steric environment of the two Cbl moieties. A biotinylated deriv. of 5-aminoisophthalate was also synthesized and used to prep. biotinylated-Cbl dimers. In a competitive rhTCII binding assay with [57Co]CN-Cbl, Cbl dimers contg. the lipophilic diaminododecane linking moiety had decreased binding avidities compared to those of Cbl monomers substituted at the same corrin ring carboxylate. However, Cbl dimers contg. the water-solubilizing trioxadiamine linker appeared to have avidities similar to those of the Cbl monomers. STcobalamin dimer prepn transcobalamin binding IT 173341-40-7P 173341-41-8P 173341-42-9P 173341-43-0P 173341-44-1P 173341-46-3P 173341-47-4P 173341-48-5P 173341-52-1P 173341-53-2P 188014-66-6P 173341-54-3P 188014-67-7P 188014-68-8P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. of cobalamin dimers and binding to human recombinant transcobalamin II) IT 12651-28-4, Transcobalamin II RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (prepn. of cobalamin dimers and binding to human recombinant transcobalamin II) ΙT 68-19-9P, Cyanocobalamin RL: PUR (Purification or recovery); PREP (Preparation)

(prepn. of cobalamin dimers and binding to human recombinant transcobalamin II)

IT 58-85-5P, Biotin 99-31-0P 26264-28-8P 38218-55-2P 38218-77-8P 160927-56-0P 173341-26-9P 173341-31-6P 173341-49-6P 173341-51-0P 173341-59-8P 188014-58-6P 188014-59-7P 188014-60-0P 188014-61-1P 188014-62-2P 188014-63-3P 188014-64-4P 188014-65-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of cobalamin dimers and binding to human recombinant transcobalamin II)

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         Jun 03 New e-mail delivery for search results now available
NEWS 10
         Jun 10 MEDLINE Reload
NEWS 11
        Jun 10 PCTFULL has been reloaded
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         Jul 02 FOREGE no longer contains STANDARDS file segment
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
                 saved answer sets no longer valid
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         Jul 29
                Enhanced polymer searching in REGISTRY
NEWS 15
         Jul 30
                NETFIRST to be removed from STN
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        Aug 08
                CANCERLIT reload
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        Aug 08
                PHARMAMarketLetter(PHARMAML) - new on STN
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        Aug 08
                NTIS has been reloaded and enhanced
NEWS 19
        Aug 19
                Aquatic Toxicity Information Retrieval (AQUIRE)
                now available on STN
NEWS 20
        Aug 19
                IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21
        Aug 19
                The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22
        Aug 26
                Sequence searching in REGISTRY enhanced
NEWS 23
        Sep 03
                JAPIO has been reloaded and enhanced
NEWS 24
        Sep 16 Experimental properties added to the REGISTRY file
NEWS 25 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 26 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27 Oct 21 EVENTLINE has been reloaded
NEWS 28 Oct 24 BEILSTEIN adds new search fields
NEWS 29 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30 Oct 25 MEDLINE SDI run of October 8, 2002
NEWS 31 Nov 18 DKILIT has been renamed APOLLIT
NEWS 32 Nov 25 More calculated properties added to REGISTRY
NEWS 33 Dec 02 TIBKAT will be removed from STN
NEWS 34 Dec 04 CSA files on STN
NEWS 35 Dec 17
                PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36 Dec 17
                TOXCENTER enhanced with additional content
NEWS 37
        Dec 17
                Adis Clinical Trials Insight now available on STN
NEWS 38
        Dec 30
                ISMEC no longer available
NEWS 39
        Jan 13 Indexing added to some pre-1967 records in CA/CAPLUS
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             CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
             AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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FULL ESTIMATED COST

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# => e aminoisophthalic

E1	8	AMINOISOPHTHALANILIDE/BI
E2	17	AMINOISOPHTHALATE/BI
E3	41>	> AMINOISOPHTHALIC/BI
E4	3	AMINOISOPHTHALO/BI
E5	1	AMINOISOPHTHALONITRILE/BI
E6	2	AMINOISOPHTHALOYL/BI
E7	3	AMINOISOPR/BI
E8	3	AMINOISOPRENE/BI
E9	3	AMINOISOPROP/BI
E10	7	AMINOISOPROPAN/BI
E11	7	AMINOISOPROPANOL/BI
E12	3	AMINOISOPROPOXY/BI

=> s e1-e6

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17 AMINOISOPHTHALATE/BI
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- 41 AMINOISOPHTHALIC/BI
- 3 AMINOISOPHTHALO/BI
- 1 AMINOISOPHTHALONITRILE/BI
- 2 AMINOISOPHTHALOYL/BI

L1 66 (AMINOISOPHTHALANILIDE/BI OR AMINOISOPHTHALATE/BI OR AMINOISOPHTHALO/BI OR AMINOISOPHTHALONITRILE/BI OR AMINOISOPHTHALOYL/BI)

=> d 11 66

L1 ANSWER 66 OF 66 REGISTRY COPYRIGHT 2003 ACS

RN 99-27-4 REGISTRY

CN 1,3-Benzenedicarboxylic acid, 5-amino-, dimethyl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Isophthalic acid, 5-amino-, dimethyl ester (7CI, 8CI)

OTHER NAMES:

CN 3,5-Dicarbomethoxyaniline

CN 5-Aminobenzene-1,3-dicarboxylic acid dimethyl ester

CN 5-Aminoisophthalic acid dimethyl ester

CN Dimethyl 5-aminobenzene-1,3-dicarboxylate

CN Dimethyl 5-aminoisophthalate

CN Methyl 5-amino-3-(methoxycarbonyl)benzoate

FS 3D CONCORD

DR 50891-97-9

MF C10 H11 N O4

CI COM

LC STN Files: BEILSTEIN\*, BIOBUSINESS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, HODOC\*, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, SPECINFO, SYNTHLINE, TOXCENTER, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, NDSL\*\*, TSCA\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

- 94 REFERENCES IN FILE CA (1962 TO DATE)
- 3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 93 REFERENCES IN FILE CAPLUS (1962 TO DATE)
- 3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d 11 1

L1 ANSWER 1 OF 66 REGISTRY COPYRIGHT 2003 ACS

RN 306305-22-6 REGISTRY

CN 1,3-Benzenedicarboxylic acid, 5-amino-, polymer with 3-aminobenzoic acid and hexahydro-2H-azepin-2-one (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2H-Azepin-2-one, hexahydro-, polymer with 5-amino-1,3-benzenedicarboxylic acid and 3-aminobenzoic acid (9CI)

CN Benzoic acid, 3-amino-, polymer with 5-amino-1,3-benzenedicarboxylic acid and hexahydro-2H-azepin-2-one (9CI)

#### OTHER NAMES:

CN m-Aminobenzoic acid-caprolactam-5-aminoisophthalic acid copolymer

MF (C8 H7 N O4 . C7 H7 N O2 . C6 H11 N O)x

CI PMS

PCT Polyamide, Polyamide formed

SR CA

LC STN Files: CA, CAPLUS

CM 1

CRN 105-60-2 CMF C6 H11 N O

CM 2

CRN 99-31-0 CMF C8 H7 N O4

CM 3

CRN 99-05-8 CMF C7 H7 N O2

- 1 REFERENCES IN FILE CA (1962 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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FILE COVERS 1907 - 16 Jan 2003 VOL 138 ISS 3 FILE LAST UPDATED: 15 Jan 2003 (20030115/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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1 BIOTINAAPFCMK/BI
2 BIOTINALYTED/BI
63 BIOTINAMIDE/BI
1 BIOTINAMIDE27/BI
1 BIOTINAMIDECAPROATE/BI
3 BIOTINAMIDES/BI E7 E8 E9 E10 E11 E12 => s e3 22854 BIOTIN/BI T.4

=> s 13 and 14

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- L5 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS
- AN 2002:523951 CAPLUS
- DN 137:228855
- TI Trifunctional conjugation reagents. Reagents that contain a biotin and a radiometal chelation moiety for application to extracorporeal affinity adsorption of radiolabeled antibodies
- AU Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.; Nilsson, Rune; Sandberg, Bengt E. B.; Brechbiel, Martin
- CS Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
- SO Bioconjugate Chemistry (2002), 13(5), 1079-1092 CODEN: BCCHES; ISSN: 1043-1802
- PB American Chemical Society
- DT Journal
- LA English
- RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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- L5 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS
- AN 2002:523951 CAPLUS
- DN 137:228855
- TI Trifunctional conjugation reagents. Reagents that contain a **biotin** and a radiometal chelation moiety for application to extracorporeal affinity adsorption of radiolabeled antibodies
- AU Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.; Nilsson, Rune; Sandberg, Bengt E. B.; Brechbiel, Martin
- CS Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
- SO Bioconjugate Chemistry (2002), 13(5), 1079-1092 CODEN: BCCHES; ISSN: 1043-1802
- PB American Chemical Society
- DT Journal
- LA English
- RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L5 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2003 ACS
- AN 2002:319261 CAPLUS
- DN 137:59601
- TI A Streptavidin-Biotin Binding System That Minimizes Blocking by Endogenous Biotin
- AU Hamblett, Kevin J.; Kegley, Brian B.; Hamlin, Don K.; Chyan, Ming-Kuan; Hyre, David E.; Press, Oliver W.; Wilbur, D. Scott; Stayton, Patrick S.
- CS Departments of Bioengineering, Medicine, and Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
- SO Bioconjugate Chemistry (2002), 13(3), 588-598 CODEN: BCCHES; ISSN: 1043-1802
- PB American Chemical Society
- DT Journal
- LA English
- RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L5 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS
- AN 2001:923565 CAPLUS

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DN
     136:42919
     Biotin derivatives for an extracorporeal device
TI
     Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune
IN
PA
     Mitra Medical Technology AB, Swed.; University of Washington
SO
     PCT Int. Appl., 45 pp.
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L5
     ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS
AN
     2000:35037 CAPLUS
     132:90367
DN
ΤI
     Trifunctional reagent for conjugation to a biomolecule for use in
     diagnosis and therapy
IN
     Wilbur, D. Scott; Sandberg, Bengt E. B.
PA
     Dept. of Radiation Oncology, University of Washington, USA; Mitra Medical
     Technology AB
SO
     PCT Int. Appl., 48 pp.
     CODEN: PIXXD2
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     English
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L5
     ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS
      2000:35036 CAPLUS
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      132:90366
DN
TI
      Trifunctional reagent for conjugation to a biomolecule for use in
      diagnosis and therapy
     Wilbur, D. Scott; Sandberg, Bengt E. B.
IN
     Department of Radiation Oncology, University of Washington, USA; Mitra
PA
     Medical Technology AB
     PCT Int. Appl., 41 pp.
SO
     CODEN: PIXXD2
DT
     Patent
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LΑ
FAN.CNT 2
                                                 APPLICATION NO.
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     WO 2000002050 A1 20000113
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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RE.CNT 11
                THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L5 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2003 ACS
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- AN 1999:668186 CAPLUS
- DN 132:46430
- TI Molecular Necklaces. Cross-Linking Hemoglobin with Reagents Containing Covalently Attached Ligands
- AU Crapatureanu, Sanda; Serbanescu, Ruxandra; Brevitt, Sharon Bisley; Kluger, Ronald
- CS Lash Miller Laboratories Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, Can.
- SO Bioconjugate Chemistry (1999), 10(6), 1058-1067 CODEN: BCCHES; ISSN: 1043-1802
- PB American Chemical Society
- DT Journal
- LA English
- OS CASREACT 132:46430
- RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L5 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2003 ACS
- AN 1999:140535 CAPLUS
- DN 130:267698
- TI Synthesis of achiral linker reagents for direct labeling of oligonucleotides on solid supports
- AU Behrens, Carsten; Dahl, Otto
- CS Department of Chemistry, University of Copenhagen, Copenhagen, DK-2100, Den.
- SO Nucleosides & Nucleotides (1999), 18(2), 291-305 CODEN: NUNUD5; ISSN: 0732-8311
- PB Marcel Dekker, Inc.
- DT Journal
- LA English
- RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L5 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2003 ACS
- AN 1999:109400 CAPLUS
- DN 130:177546
- ${\tt TI}$  Methods of receptor modulation and therapeutic and diagnostic uses therefor
- IN Morgan, A. Charles, Jr.; Wilbur, D. Scott
- PA Receptagen Corporation, USA; University of Washington
- SO U.S., 47 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned. CODEN: USXXAM
- DT Patent
- LA English
- FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5869465	A	19990209	US 1995-406194	19950316
	CA 2187346	AA	19951019	CA 1995-2187346	19950407
	WO 9527723	A1	19951019	WO 1995-US4404	19950407
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	US 6083926	A	20000704	US 1998-200422	19981123

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    US 1995-545151 A3 19951019
RE.CNT 19
             THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
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    ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS
AN
     1998:776603 CAPLUS
DN
    130:38642
ΤI
    Preparation of water soluble vitamin B12 as antiinflammatory receptor
    modulating agents
IN
    Morgan, A. Charles, Jr.; Wilbur, D. Scott
PΑ
    Receptagen Corporation, USA; University of Washington
SO
    U.S., 50 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned.
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    US 5840880 A 19981124 US 1995-406191 19950316
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    1998:776598 CAPLUS
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    130:38641
    Preparation of water soluble vitamin B12 as antiinflammatory receptor
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    Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
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    Receptagen Corporation, USA; University of Washington
    U.S., 66 pp., Cont.-in-part of U.S. Ser. No. 406,191.
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    1998:236288 CAPLUS
AN
DN
     128:295003
     Preparation of biotinylated cobalamins as antiinflammatory agents and
     transcobalamin II receptors
IN
    Wilbur, D. Scott; Pathare, Pradip M.; Morgan, A. Charles, Jr.
PΑ
    University of Washington, USA; Receptagen Corp.
SO
    U.S., 58 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned.
     CODEN: USXXAM
DT
    Patent
    English
LA
FAN.CNT 6
    PATENT NO.
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                                        APPLICATION NO. DATE
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PΙ
    US 5739287
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                                                          19950316
    CA 2187346
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                                         CA 1995-2187346 19950407
                 A1 19951019
    WO 9527723
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                                                          19950407
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A
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    US 5840712
                                         US 1995-545151
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    US 6083926
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                                         US 1998-200422
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PRAI US 1994-224831
                          19940408
    US 1995-406191 A
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    US 1995-406192
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                           19950316
    US 1995-406194 A
                          19950316
    WO 1995-US4404
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    US 1995-545151
                   A3 19951019
    ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS
L5
AN
    1997:377886 CAPLUS
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126:343813
DN
     Preparation of vitamin B12 receptor modulating agents
ΤI
     Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
IN
PA
     Receptagen Corporation, USA; University of Washington; Morgan, A. Charles,
     Jr.; Wilbur, D. Scott; Pathare, Pradip, M.
     PCT Int. Appl., 97 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 6
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                            DATE
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     WO 9714711
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     US 1995-406194
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     WO 1996-US16672
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os
     MARPAT 126:343813
L5
     ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS
     1997:251007 CAPLUS
AN
DN
     126:238622
ΤI
     A new achiral linker reagent for the incorporation of multiple amino
     groups into oligonucleotides
IN
     Behrens, Carsten; Petersen, Kenneth H.; Egholm, Michael; Nielsen, John;
     Dahl, Otto
PA
     Behrens, Carsten, Den.; Petersen, Kenneth H.; Egholm, Michael; Nielsen,
     John; Dahl, Otto
     PCT Int. Appl., 34 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
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                      KIND DATE
                                            APPLICATION NO.
                                                              DATE
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PRAI DK 1995-863
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OS
    MARPAT 126:238622
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L5
    ANSWER 14 OF 15 CAPLUS COPYRIGHT 2003 ACS
AN
    1997:155067 CAPLUS
    126:207193
DN
     Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin
TI
     Ring Carboxylates and Evaluation of Their Binding to Transcobalamin. 2
     Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon;
ΑU
     Quadros, Edward V.; McLoughlin, Patricia; Morgan, A. Charles
CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
     Bioconjugate Chemistry (1997), 8(2), 161-172
SO
     CODEN: BCCHES; ISSN: 1043-1802
    American Chemical Society
PB
DT
    Journal
LA
    English
Ļ5
    ANSWER 15 OF 15 CAPLUS COPYRIGHT 2003 ACS
AN
    1991:225167 CAPLUS
DN
    114:225167
    Method of assaying substances and immunoassay element employing
    .beta.-D-galactosidase
IN
    Onishi, Akira; Kawakatsu, Satoshi; Ito, Tsukasa; Takahashi, Takenori;
     Fukaya, Michie
PΑ
    Konica Co., Japan
    Eur. Pat. Appl., 61 pp.
SO
    CODEN: EPXXDW
DT
     Patent
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m LA}
    English
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                                         APPLICATION NO. DATE
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PΙ
    EP 328106
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                     A2 19891213
                                        JP 1989-31530
                                                          19890209
     JP 01308967
                      A2 19891213
                                         JP 1989-31531
                                                          19890209
PRAI JP 1988-29632
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    JP 1988-29633
                           19880209
OS
    MARPAT 114:225167
=> d 15 3-15 all
    ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS
AN
    2001:923565 CAPLUS
DN
    136:42919
    Biotin derivatives for an extracorporeal device
TI
    Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune
IN
PΑ
    Mitra Medical Technology AB, Swed.; University of Washington
SO
    PCT Int. Appl., 45 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
    ICM A61K
IC
     63-7 (Pharmaceuticals)
    Section cross-reference(s): 26
FAN.CNT 1
    PATENT NO.
                   KIND DATE
                                         APPLICATION NO. DATE
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PΙ
    WO 2001095857
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                    A3 20020328
        W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
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CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,

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             MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ,
             TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,
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             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 2002159994
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                            20021031
                                           US 2001-881213
                                                             20010615
     AU 2001074761
                       Α5
                            20011224
                                           AU 2001-74761
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PRAI SE 2000-2287
                       Α
                            20000616
     US 2000-216625P
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     WO 2001-SE1374
                       W
                            20010618
AΒ
     A method for the conditioning of an extracorporeal device is described, as
     well as a method for extracorporeal extn. of toxic material from mammalian
     body fluids in connection with diagnosis or treatment of a mammalian
     condition or disease. The methods comprise (i) a soln. contg. a reagent
     comprising biotin moieties, such as natural biotin or
     its derivs., and a toxin-binding moiety, (ii) linkers and a trifunctional
     crosslinking moiety, and (ii) an extracorporeal device comprising said
     reagent. For example, a dibiotin compd., 1-isothiocyanato-3,5-bis-(13'-
     biotinamidyl-4',7',10'-trioxatridecanamidyl)-aminoisophthalate was prepd.
     and conjugated with a toxin-binding mol., i.e., monoclonal antibody
     53-6A2. A dibiotin-toxin-binding conjugate was used for conditioning of
     an avidin-agarose column suitable for removal of toxins from blood.
ST
     biotin deriv prepn reagent extracorporeal toxin extn; body fluid
     toxin extn extracorporeal biotin reagent
IT
     Histocompatibility antigens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (HLA, antibodies against; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Imaging
        (NMR; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids in diagnosis and therapy)
IT
     Intercalation
        (agents; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
ΙT
     Antibodies
     RL: REM (Removal or disposal); PROC (Process)
        (anti-blood group; prepn. of biotin derivs. for conditioning
        of extracorporeal device and extn. of toxic material from mammalian
        body fluids)
IT
     Blood-group substances
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (antibodies against; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Avidins
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (biotin derivs.-binding coatings; prepn. of biotin
        derivs. for conditioning of extracorporeal device and extn. of toxic
        material from mammalian body fluids)
IT
     Immunity
        (cells involved in, removal of; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic material from
        mammalian body fluids)
TΨ
     Avidins
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
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study); USES (Uses)
        (conjugates, with agarose; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
    Animal cell
        (diseased, removal of; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     RL: REM (Removal or disposal); PROC (Process)
        (endotoxins; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
IT
    Toxins
     RL: REM (Removal or disposal); PROC (Process)
        (enterotoxins; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
ΙT
    Circulation
     Extraction
        (extracorporeal; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
ΙT
     Chelating agents
        (for radionuclides; prepn. of biotin derivs. for conditioning
        of extracorporeal device and extn. of toxic material from mammalian
        body fluids)
IT
     Immunoglobulins
     RL: REM (Removal or disposal); PROC (Process)
        (fragments; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
ΙT
    Antibodies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (monoclonal, conjugates, with dibiotin compd.; prepn. of biotin
        derivs. for conditioning of extracorporeal device and extn. of toxic
        material from mammalian body fluids)
ΤТ
    Antibodies
    RL: REM (Removal or disposal); PROC (Process)
        (monoclonal; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
IT
    Amino group
    Blood
    Body fluid
    Carboxyl group
    Chemotherapy
    Cytotoxic agents
    Dyes
    Extraction columns
    Hydroxyl group
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
ΙT
    Chelates
    Cytokines
    Metals, processes
    Oligodeoxyribonucleotides
    Peptides, processes
    Radionuclides, processes
    Toxins
    Tumor necrosis factors
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RL: REM (Removal or disposal); PROC (Process)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
     Diagnosis
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids in
        diagnosis and disease treatment)
     Positron-emission tomography
IT
     Scintigraphy
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids in
        diagnosis and therapy)
IT
     Transplant and Transplantation
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids prior to
        transplantation)
IT
     Bacteria (Eubacteria)
     Virus
        (toxins; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
IT
     Disease, animal
        (treatment; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids in diagnosis and disease treatment)
IT
     Reagents
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (tribiotinylated; prepn. of biotin derivs. for conditioning
        of extracorporeal device and extn. of toxic material from mammalian
        body fluids)
IT
     Neoplasm
        (uptake, monitoring of; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic material from
        mammalian body fluids)
     Antibodies
TТ
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (xenoantibodies, antibodies against; prepn. of biotin derivs.
        for conditioning of extracorporeal device and extn. of toxic material
        from mammalian body fluids)
TΤ
     9013-20-1, Streptavidin
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (biotin derivs.-binding coatings; prepn. of biotin
        derivs. for conditioning of extracorporeal device and extn. of toxic
        material from mammalian body fluids)
IT
     9012-36-6D, Agarose, conjugates with avidin
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
     58-85-5, Biotin 99-31-0, 5-Aminoisophthalic acid
     4246-51-9, 4,7,10,Trioxa-1,13-tridecanediamine 24424-99-5, Di-tert-butyl
     dicarbonate
                  142685-25-4, 2,3,5,6-Tetrafluorophenyl trifluoroacetate
     380607-49-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of biotin derivs. for conditioning of extracorporeal
       device and extn. of toxic material from mammalian body fluids)
TΤ
     173341-32-7P
                   178446~63-4P
                                  183896-00-6P
                                                  380607-50-1P
                                                                 380607-51-2P
                    380607-60-3P
     380607-56-7P
                                   380607-61-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of biotin derivs. for conditioning of extracorporeal
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device and extn. of toxic material from mammalian body fluids)
ΙT
     380607-52-3P
                     380607-54-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
     USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
     194920-56-4P
ΙT
                    194920-58-6P
                                   380607-48-7P
                                                   380607-52-3DP, conjugates
                                                                  380607-57-8P
     with monoclonal antibodies
                                    380607-53-4P
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     380607-58-9P
                    380607-59-0P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
         (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
     533-48-2, Desthiobiotin 535-87-5, 3,5-Diaminobenzoic acid 554-95-0,
     1,3,5-Benzene tricarboxylic acid 669-72-7, Nor-biotin
     1784-22-1, Homobiotin 3376-83-8, Biotin sulfoxide
     13395-35-2, Iminobiotin 14474-91-0, Oxybiotin
     Diaminobiotin
                      40720-05-6, Biotin sulfone
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
ΙT
     58-85-5D, Biotin, derivs.
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (radiolabeled; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
L5
     ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS
AN
     2000:35037 CAPLUS
DN
     132:90367
     Trifunctional reagent for conjugation to a biomolecule for use in
TI
     diagnosis and therapy
IN
     Wilbur, D. Scott; Sandberg, Bengt E. B.
PA
     Dept. of Radiation Oncology, University of Washington, USA; Mitra Medical
     Technology AB
SO
     PCT Int. Appl., 48 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM G01N033-543
     ICS A61K039-00; A61K047-48; A61K051-00; A61K049-00
     9-15 (Biochemical Methods)
     Section cross-reference(s): 1, 8, 15, 63
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PΙ
     WO 2000002051
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             SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     WO 2000002050
                      A1 20000113
                                           WO 1998-SE1345
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             CM, GA, GN, ML, MR, NE, SN, TD, TG
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                                           US 2000-750280
                                                            20001229
     NO 2001000021
                      Α
                            20010307
                                           NO 2001-21
                                                            20010103
PRAI WO 1998-SE1345
                       Α
                            19980707
     WO 1999-SE1241
                       W
                            19990707
     A reagent for conjugation to a biomol. for diagnosis and treatment of
AB
     human and animal conditions and diseases is described, wherein the reagent
     is a single mol. with at least three functional parts and a) wherein a
     trifunctional crosslinking moiety is coupled to b) an affinity ligand via
     a linker 1, said affinity ligand being capable of binding with another
     mol. having affinity for said ligand; to c) an effector agent, optionally
     via a linker 2, said effector agent exerting its effects on cells, tissues
     and/or humorous mols. in vivo or ex vivo; and to d) a biomol. reactive
     moiety, optionally via a linker 3, said moiety being capable of forming a
     bond between the reagent and the biomol. The affinity ligand is esp.
     biotin or a biotin deriv. The effector agent is a
     toxin, an enzyme capable of converting a prodrug to an active drug, an
     immunosuppressant, an immunostimulant, or a radionuclide-binding agent,
     with or without the radionuclide.
ST
     trifunctional reagent biomol conjugation diagnosis therapy; biotin
     trifunctional reagent biomol conjugate diagnosis therapy; toxin
     trifunctional reagent biomol conjugate therapy; prodrug converting enzyme
     trifunctional reagent conjugate; immunomodulator trifunctional reagent
     conjugate; radiotherapy trifunctional reagent conjugate; imaging agent
     trifunctional reagent conjugate
ΙT
     Imaging agents
        (NMR contrast, trifunctional reagent contq., as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
TΤ
     Imaging agents
        (acoustic imaging contrast agents, trifunctional reagent contg., as
        effector agent; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     Proteins, specific or class
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (affinity ligand-binding, for removal of nontargeted biomol. conjugate
        from blood circulation; trifunctional reagent for conjugation to a
        biomol. for use in diagnosis and therapy)
IT
     Ligands
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); PROC (Process); USES (Uses)
        (affinity, trifunctional reagent contg.; trifunctional reagent for
        conjugation to a biomol. for use in diagnosis and therapy)
IT
     Functional groups
        (ammonio group, linkers contg.; trifunctional reagent for conjugation
        to a biomol. for use in diagnosis and therapy)
IT
     Chromophores
     Fluorescent substances
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(as effector agent in trifunctional reagent; trifunctional reagent for

conjugation to a biomol. for use in diagnosis and therapy)

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IT
     Separators
        (blood plasma, in kit for removal of nontargeted biomol. conjugate from
        blood circulation; trifunctional reagent for conjugation to a biomol.
        for use in diagnosis and therapy)
     Amines, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (cyclic, radionuclide-binding, as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
ΙT
     Lung, disease
        (embolism; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
ΙT
     Carboxylic acids, properties
     RL: PRP (Properties)
        (esters, linkers contg.; trifunctional reagent for conjugation to a
        biomol. for use in diagnosis and therapy)
IT
     Adsorption apparatus
        (extracorporeal, in kit for removal of nontargeted biomol. conjugate
        from blood circulation; trifunctional reagent for conjugation to a
        biomol. for use in diagnosis and therapy)
TT
        (extracorporeal, nontargeted biomol. conjugate removal from;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
     Affinity chromatographic stationary phases
IT
        (for removal of nontargeted biomol. conjugate from blood circulation;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Imaging
        (gamma-ray; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
     Vinyl compounds, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (halo, halogen radionuclide-contg., as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Aryl halides
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (halogen radionuclide-contg., as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
    Avidins
     Receptors
     RL: BUU (Biological use, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (immobilized, extracorporeal adsorption device contq., in kit for
        removal of nontargeted biomol. conjugate from blood circulation;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
    Heart, disease
IT
        (infarction; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
TI
     Ethers, properties
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Sulfonates
     Thioethers
     RL: PRP (Properties)
        (linkers contg.; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
ΙT
     Circulation
        (nontargeted biomol. conjugate removal from; trifunctional reagent for
        conjugation to a biomol. for use in diagnosis and therapy)
     Radiosensitizers, biological
IT
        (pharmaceutical, trifunctional reagent contq., as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Materials
        (photoactive chems., as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Enzymes, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (prodrug-metabolizing, trifunctional reagent contg., as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Drug delivery systems
        (prodrugs, trifunctional reagent contg. enzymes metabolizing;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Brain, disease
        (stroke; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Radiotherapy
        (targeted; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
IT
     Disease, animal
        (treatment of; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     Avidins
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (trifunctional reagent contg. affinity ligand binding to; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
ΙT
     Body fluid
        (trifunctional reagent contg. effector agent acting on mols. in;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
    Animal tissue
ΙT
     Cell
        (trifunctional reagent contg. effector agent acting on; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
ΙT
     Radionuclides, biological studies
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (trifunctional reagent contg. moieties binding to, as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Immunostimulants
     Immunosuppressants
        (trifunctional reagent contg., as effector agent; trifunctional reagent
        for conjugation to a biomol. for use in diagnosis and therapy)
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IT
     Enzymes, biological studies
     Hormones, animal, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (trifunctional reagent contg., as effector agent; trifunctional reagent
        for conjugation to a biomol. for use in diagnosis and therapy)
IT
     Animal
     Atherosclerosis
     Biochemical molecules
     Diagnosis
     Drug targeting
     Mammal (Mammalia)
     Neoplasm
     Photodynamic therapy
     Photoimaging
     Positron-emission tomography
     Therapy
     Vertebrate (Vertebrata)
        (trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Reagents
     RL: ARG (Analytical reagent use); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); RACT (Reactant or
     reagent); USES (Uses)
        (trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
ΙT
     Crosslinking agents
        (trifunctional; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     Thrombosis
        (venous, deep; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
ΙT
     Imaging agents
        (x-ray, contrast, trifunctional reagent contq., as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     9025-15-4, Biotinidase
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (biotin-contg. reagent with stability against cleavage with;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     7439-92-1D, Lead, radionuclides, biological studies
                                                           7439-94-3D,
     Lutetium, radionuclides, biological studies 7440-19-9D, Samarium,
     radionuclides, biological studies 7440-50-8D, Copper, radionuclides,
     biological studies 7440-65-5D, Yttrium, radionuclides, biological
              7440-69-9D, Bismuth, radionuclides, biological studies
     7440-74-6D, Indium, radionuclides, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (cyclic amines binding to, as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
TΤ
     15715-08-9, Iodine-123, biological studies
                                                  15750-15-9, Indium-111,
    biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
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ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for gamma ray
        imaging; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
     13981-56-1, Fluorine-18, biological studies
                                                 14158-30-6, Iodine-124,
TΤ
    biological studies 14809-47-3, Bromine-75, biological studies
     15765-38-5, Bromine-76, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for positron imaging;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     10043-66-0, Iodine-131, biological studies
                                                 10098-91-6, Yttrium-90,
                          14265-75-9, Lutetium-177, biological studies
    biological studies
     14378-26-8, Rhenium-188, biological studies 14913-49-6, Bismuth-212,
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    biological studies
     15623-45-7, Radium-223, biological studies
                                                 15755-39-2, Astatine-211,
                          15757-86-5, Copper-67, biological studies
    biological studies
     15776-20-2, Bismuth-213, biological studies
                                                   29687-57-8, Samarium-157,
    biological studies
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for radiotherapy;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     9013-20-1D, Streptavidin, immobilized
     RL: BUU (Biological use, unclassified); DEV (Device component use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (extracorporeal adsorption device contg., in kit for removal of
        nontargeted biomol. conjugate from blood circulation; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
TΤ
     14133-76-7, Technetium-99, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (metastable, effector agent contg., in trifunctional reagent, for gamma
        ray imaging; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
TΤ
     13981-55-0, Indium-114, biological studies
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (metastable, effector agent contg., in trifunctional reagent, for
        radiotherapy; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
     60-00-4D, EDTA, derivs.
                               67-43-6D, DTPA, derivs.
ΙT
                                                         3565-84-2
     56491-86-2, NOTA
                       60239-18-1, DOTA 60239-22-7, TETA
                                                              254441-22-0
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (radionuclide-binding, as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
    9013-20-1, Streptavidin
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RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (trifunctional reagent contg. affinity ligand binding to; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy) 58-85-5D, Biotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 99-31-0D, 3,5-Dicarboxyaniline, conjugates with affinity ligand and effector agent and biomol. reactive moiety 108-72-5D, 1,3,5-Triaminobenzene, conjugates with affinity ligand and effector agent and biomol. reactive moiety 533-48-2D, Desthiobiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 535-87-5D, 3,5-Diaminobenzoic acid, conjugates with affinity ligand and effector agent and biomol. reactive moiety 554-95-0D, 1,3,5-Tricarboxybenzene, conjugates with affinity ligand and effector agent and biomol. reactive 669-72-7D, Norbiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 1784-22-1D, Homobiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 3376-83-8D, Biotin sulfoxide, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 13395-35-2D, Iminobiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 14474-91-0D, Oxybiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 22342-46-7D, Diaminobiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 40720-05-6D, Biotin sulfone, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 254441-23-1 254441-24-2D, derivs. 254441-25-3 254441-26-4 254441-28-6 254447-29-5 254447-31-9 RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses) (trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy) RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Beckman Instruments Inc; EP 0310361 A2 1989 CAPLUS (2) Board Of Regents Of The University Of Washington; WO 9729114 A1 1997 CAPLUS (3) Boehringer Mannheim Gmbh; EP 0618192 A1 1994 CAPLUS (4) Cancer Research Campaign Technology Limited; WO 8910140 A1 1989 CAPLUS (5) Eigo, O; 1997, 20, CAPLUS (6) Eigo, O; Cancer Res 1997, V88(2), P205 (7) Gaetjens, E; US 5134071 A 1992 CAPLUS (8) Hybritech Incorporated; WO 9302105 A1 1993 CAPLUS (9) Immunomedics Inc; WO 9604313 A1 1996 CAPLUS (10) Jacobson, K; US 5310916 A 1994 CAPLUS (11) Muzykantov, V; Proc Natl Acad Sci 1996, V93, P5213 CAPLUS (12) Pharmacia & Upjohn Ab; WO 9904820 A2 1999 CAPLUS (13) Tutt, A; The Journal of Immunology 1991, V147(1), P60 CAPLUS ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS 2000:35036 CAPLUS 132:90366 Trifunctional reagent for conjugation to a biomolecule for use in

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RE

- TΙ diagnosis and therapy
- IN Wilbur, D. Scott; Sandberg, Bengt E. B.
- PΑ Department of Radiation Oncology, University of Washington, USA; Mitra Medical Technology AB
- SO PCT Int. Appl., 41 pp. CODEN: PIXXD2
- DΤ Patent
- LΑ English

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IC
     ICM G01N033-543
     ICS C07K019-00; A61K039-395; A61K047-48; A61K051-00; A61K049-00
     9-15 (Biochemical Methods)
     Section cross-reference(s): 1, 8, 15, 63
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     WO 1999-SE1241
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AΒ
     A reagent for conjugation to a biomol. for diagnosis and treatment of
     human and animal conditions and diseases is described, wherein the reagent
     is a single mol. with at least three functional parts and a) wherein a
     trifunctional crosslinking moiety is coupled to b) an affinity ligand via
     a linker 1, said affinity ligand being capable of binding with another
     mol. having affinity for said ligand; to c) an effector agent, optionally
     via a linker 2, said effector agent exerting its effects on cells, tissues
     and/or humorous mols. in vivo or ex vivo; and to d) a biomol. reactive
     moiety, optionally via a linker 3, said moiety being capable of forming a
     bond between the reagent and the biomol. The affinity ligand is esp.
     biotin or a biotin deriv. The effector agent is a
     toxin, an enzyme capable of converting a prodrug to an active drug, an
    immunosuppressant, an immunostimulant, or a radionuclide-binding agent,
     with or without the radionuclide.
     trifunctional reagent biomol conjugation diagnosis therapy; biotin
ST
     trifunctional reagent biomol conjugate diagnosis therapy; toxin
     trifunctional reagent biomol conjugate therapy; prodrug converting enzyme
     trifunctional reagent conjugate; immunomodulator trifunctional reagent
     conjugate; radiotherapy trifunctional reagent conjugate; imaging agent
     trifunctional reagent conjugate
IT
     Proteins, specific or class
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (affinity ligand-binding, for removal of nontargeted biomol. conjugate
        from blood circulation; trifunctional reagent for conjugation to a
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biomol. for use in diagnosis and therapy)
IT
     Ligands
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); PROC (Process); USES (Uses)
        (affinity, trifunctional reagent contq.; trifunctional reagent for
        conjugation to a biomol. for use in diagnosis and therapy)
IT
     Functional groups
        (ammonio group, linkers contq.; trifunctional reagent for conjugation
        to a biomol. for use in diagnosis and therapy)
IT
     Separators
        (blood plasma, in kit for removal of nontargeted biomol. conjugate from
        blood circulation; trifunctional reagent for conjugation to a biomol.
        for use in diagnosis and therapy)
IT
     Amines, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (cyclic, radionuclide-binding, as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Lung, disease
        (embolism; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
IT
     Carboxylic acids, properties
     RL: PRP (Properties)
        (esters, linkers contg.; trifunctional reagent for conjugation to a
        biomol. for use in diagnosis and therapy)
IT
     Adsorption apparatus
        (extracorporeal, in kit for removal of nontargeted biomol. conjugate
        from blood circulation; trifunctional reagent for conjugation to a
        biomol. for use in diagnosis and therapy)
TT
     Circulation
        (extracorporeal, nontargeted biomol. conjugate removal from;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
TТ
     Affinity chromatographic stationary phases
        (for removal of nontargeted biomol. conjugate from blood circulation;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΤТ
     Imaging
        (gamma-ray; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
     Vinyl compounds, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (halo, halogen radionuclide-contg., as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
ΤТ
     Aryl halides
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (halogen radionuclide-contg., as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
    Avidins
    Receptors
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RL: BUU (Biological use, unclassified); DEV (Device component use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (immobilized, extracorporeal adsorption device contg., in kit for
        removal of nontargeted biomol. conjugate from blood circulation;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Heart, disease
        (infarction; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
ΙT
     Ethers, properties
     Sulfonates
     Thioethers
     RL: PRP (Properties)
        (linkers contg.; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
TΨ
     Circulation
        (nontargeted biomol. conjugate removal from; trifunctional reagent for
        conjugation to a biomol. for use in diagnosis and therapy)
IT
     Enzymes, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (prodrug-metabolizing, trifunctional reagent contg., as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Drug delivery systems
        (prodrugs, trifunctional reagent contg. enzymes metabolizing;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Brain, disease
        (stroke; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
     Radiotherapy
IT
        (targeted; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
IT
     Disease, animal
        (treatment of; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
    Avidins
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (trifunctional reagent contg. affinity ligand binding to; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
ΙT
     Body fluid
        (trifunctional reagent contg. effector agent acting on mols. in;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
    Animal tissue
ΙT
     Cell
        (trifunctional reagent contg. effector agent acting on; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
IT
     Radionuclides, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (trifunctional reagent contg. moieties binding to, as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Immunostimulants
     Immunosuppressants
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(trifunctional reagent contg., as effector agent; trifunctional reagent
        for conjugation to a biomol. for use in diagnosis and therapy)
IT
     Enzymes, biological studies
     Toxins
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (trifunctional reagent contg., as effector agent; trifunctional reagent
        for conjugation to a biomol. for use in diagnosis and therapy)
TT
     Animal
     Atherosclerosis
     Biochemical molecules
     Diagnosis
     Drug targeting
     Mammal (Mammalia)
     Neoplasm
     Positron-emission tomography
     Therapy
     Vertebrate (Vertebrata)
        (trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Reagents
     RL: ARG (Analytical reagent use); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); RACT (Reactant or
     reagent); USES (Uses)
        (trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Crosslinking agents
        (trifunctional; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
        (venous, deep; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     9025-15-4, Biotinidase
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (biotin-contg. reagent with stability against cleavage with;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
    7439-92-1D, Lead, radionuclides, biological studies
                                                           7439-94-3D.
     Lutetium, radionuclides, biological studies
                                                  7440-19-9D, Samarium,
     radionuclides, biological studies
                                         7440-50-8D, Copper, radionuclides,
     biological studies
                         7440-65-5D, Yttrium, radionuclides, biological
               7440-69-9D, Bismuth, radionuclides, biological studies
     7440-74-6D, Indium, radionuclides, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (cyclic amines binding to, as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     15715-08-9, Iodine-123, biological studies 15750-15-9, Indium-111,
     biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for gamma ray
        imaging; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
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ΙT
     13981-56-1, Fluorine-18, biological studies
                                                  14158-30-6, Iodine-124,
     biological studies 14809-47-3, Bromine-75, biological studies
     15765-38-5, Bromine-76, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for positron imaging;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     10043-66-0, Iodine-131, biological studies
                                                  10098-91-6, Yttrium-90,
     biological studies
                         14265-75-9, Lutetium-177, biological studies
     14378-26-8, Rhenium-188, biological studies 14913-49-6, Bismuth-212,
     biological studies
                          14998-63-1, Rhenium-186, biological studies
     15623-45-7, Radium-223, biological studies
                                                 15755-39-2, Astatine-211,
                         15757-86-5, Copper-67, biological studies
     biological studies
     15776-20-2, Bismuth-213, biological studies 29687-57-8, Samarium-157,
     biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for radiotherapy;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
     9013-20-1D, Streptavidin, immobilized
IT
     RL: BUU (Biological use, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (extracorporeal adsorption device contg., in kit for removal of
        nontargeted biomol. conjugate from blood circulation; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
     14133-76-7, Technetium-99, biological studies
ΙT
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (metastable, effector agent contg., in trifunctional reagent, for gamma
        ray imaging; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
IT
     13981-55-0, Indium-114, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (metastable, effector agent contg., in trifunctional reagent, for
        radiotherapy; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     60-00-4D, EDTA, derivs. 67-43-6D, DTPA, derivs.
                                                          3565-84-2
                      60239-18-1, DOTA 60239-22-7, TETA
     56491-86-2, NOTA
                                                              254441-22-0
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (radionuclide-binding, as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     9013-20-1, Streptavidin
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (trifunctional reagent contg. affinity ligand binding to; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
IT
     58-85-5D, Biotin, conjugates with crosslinking agent binding to
```

effect agent and to biomol. reactive moiety 99-31-0D, 3,5-Dicarboxyaniline, conjugates with affinity ligand and effector agent and biomol. reactive moiety 108-72-5D, 1,3,5-Triaminobenzene, conjugates with affinity ligand and effector agent and biomol. reactive moiety 533-48-2D, Desthiobiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 535-87-5D, 3,5-Diaminobenzoic acid, conjugates with affinity ligand and effector agent and biomol. reactive moiety 554-95-0D, 1,3,5-Tricarboxybenzene, conjugates with affinity ligand and effector agent and biomol. reactive 669-72-7D, Norbiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 1784-22-1D, Homobiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 3376-83-8D, Biotin sulfoxide, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 13395-35-2D, Iminobiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 14474-91-0D, Oxybiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 22342-46-7D, Diaminobiotin, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 40720-05-6D, Biotin sulfone, conjugates with crosslinking agent binding to effect agent and to biomol. reactive moiety 254441-23-1 254441-24-2D, derivs. 254441-25-3 254441-26-4 254441-28-6 254447-29-5 RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses) (trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy) THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE.CNT RE

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- (2) Board Of Regents Of The University Of Washington; WO 9729114 A1 1997 CAPLUS
- (3) Boehringer Mannheim Gmbh; EP 0618192 A1 1994 CAPLUS
- (4) Cancer Research Campaign Technology Limited; WO 8910140 A1 1989 CAPLUS
- (5) Gaetjens, E; US 5134071 A 1992 CAPLUS
- (6) Hybritech Incorporated; WO 9302105 A1 1993 CAPLUS
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- L5 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2003 ACS
- 1999:668186 CAPLUS AN
- DN 132:46430
- TΤ Molecular Necklaces. Cross-Linking Hemoglobin with Reagents Containing Covalently Attached Ligands
- ΑU Crapatureanu, Sanda; Serbanescu, Ruxandra; Brevitt, Sharon Bisley; Kluger, Ronald
- CS Lash Miller Laboratories Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, Can.
- SO Bioconjugate Chemistry (1999), 10(6), 1058-1067 CODEN: BCCHES; ISSN: 1043-1802
- PΒ American Chemical Society
- DΤ Journal
- LΑ English
- CC 6-3 (General Biochemistry) Section cross-reference(s): 9
- OS CASREACT 132:46430
- Hb can be cross-linked and converted to a bioconjugate in one step by a AΒ mol. necklace, a reagent that contains two reacting sites and a pendant

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ligand. The compd. to be conjugated is activated as an electrophile.
     activated material is then combined with a reagent (3-aminoisophthalic
     acid) that contains a nucleophilic (amino) site and two latent (carboxyl)
     sites. The latent sites of the product are activated as
     3,5-dibromosalicylates to produce the cross-linker. Illustrative examples
     of crosslinking are presented with pendant biotin
     [bis(3,5-dibromosalicyl) N-biotinyl-5-aminoisophthalate] and pendant
     N-trifluoroacetyl-L-isoleucylglycine [bis(3,5-dibromosalicyl)
     N-(N-trifluoroacetyl-L-isoleucylglycyl)-5-aminoisophthalate].
     resulting modified Hbs contain two principal types of cross-link:
     (.beta.-Lys-82-.beta.'-Lys-82) and (.alpha.-Lys-99-.alpha.'-Lys-99).
     functional properties of the modified Hb contg. biotin in a
     (.beta.-Lys-82-.beta.'-Lys-82) cross-link are (pH 7.4, 55 .mu.M heme, 25
     .degree.C, 0.1 M chloride, and 50 mM Bis-Tris) P50 = 4.9 Torr, n50 = 3.0,
     values which are approx. the same as for native Hb. The results of
     affinity chromatog. of the biotinylated cross-linked Hb using a column of
     immobilized avidin indicate that the pendant biotin is much less
     accessible than free biotin. We suggest that the results are
     consistent with the pendant species being strongly attracted into the Hb
     Hb crosslinking bioconjugate mol necklace pendant ligand
     Hemoglobins
     RL: BPR (Biological process); BSU (Biological study, unclassified); PRP
     (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP
     (Preparation); PROC (Process)
        (crosslinked, bioconjugates; prepn. of mol. necklaces contq. pendant
        ligands for crosslinking of Hb to make bioconjugates)
     Crosslinking
        (prepn. of mol. necklaces contq. pendant ligands for crosslinking of Hb
        to make bioconjugates)
     Hemoglobins
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of mol. necklaces contg. pendant ligands for crosslinking of Hb
        to make bioconjugates)
     7782-44-7, Oxygen, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (binding by Hb bioconjugates; prepn. of mol. necklaces contg. pendant
        ligands for crosslinking of Hb to make bioconjugates)
     56-87-1, L-Lysine, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (crosslinking; prepn. of mol. necklaces contg. pendant ligands for
        crosslinking of Hb to make bioconjugates)
     25952-53-8, 1-(3-Dimethylaminopropyl)3-ethylcarbodiimide hydrochloride
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (linker; prepn. of mol. necklaces contg. pendant ligands for
        crosslinking of Hb to make bioconjugates)
     58-85-5 99-27-4, Dimethyl 5-aminoisophthalate 99-31-0,
     5-Aminoisophthalic acid 407-25-0, Trifluoroacetic acid anhydride
     7719-09-7, Thionyl chloride
                                  16257-05-9
                                                88797-22-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of mol. necklaces contg. pendant ligands for crosslinking of Hb
        to make bioconjugates)
     91853-90-6P
                   252861-79-3P
                                  252861-80-6P
                                                 252861-81-7P
                                                                252861-82-8P
     252861-83-9P
                    252861-84-0P
                                   252861-85-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of mol. necklaces contg. pendant ligands for crosslinking of Hb
        to make bioconjugates)
RE.CNT
       29
             THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
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- (27) Trimble, S; Bioconjugate Chem 1997, V8, P416 CAPLUS
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- L5 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2003 ACS
- AN 1999:140535 CAPLUS
- DN 130:267698
- TI Synthesis of achiral linker reagents for direct labeling of oligonucleotides on solid supports
- AU Behrens, Carsten; Dahl, Otto
- CS Department of Chemistry, University of Copenhagen, Copenhagen, DK-2100, Den.
- SO Nucleosides & Nucleotides (1999), 18(2), 291-305 CODEN: NUNUD5; ISSN: 0732-8311
- PB Marcel Dekker, Inc.
- DT Journal
- LA English
- CC 33-10 (Carbohydrates)
  - Section cross-reference(s): 9
- AB Full exptl. procedures for the synthesis of a series of new functional linker reagents and solid supports are reported. The achiral linker reagents and supports can be used for high yield incorporation of free amino groups, fluorescein or **biotin** into DNA oligomers.
- ST achiral amino linker oligonucleotide solidphase prepn fluorescent label; hybridization oligonucleotide achiral amino linker
- IT Solid phase synthesis
  - (of oligonucleotides contg. achiral amino linker reagents for direct labeling)
- IT Nucleic acid hybridization
  - (of oligonucleotides contg. achiral amino linker units)
- IT Fluorescent substances
  - (prepn. of using achiral amino linker reagents for direct labeling of oligonucleotides)
- IT Oligonucleotides
  - RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP

```
(synthesis of achiral amino linker reagents for direct labeling of
        oligonucleotides on solid supports)
ΙT
     99-31-0P 42122-73-6P
                            71176-54-0P
                                          146335-23-1P
     147190-36-1P 171082-06-7P 171082-07-8P 171082-08-9DP,
     solid-supported 171082-09-0P
                                      188257-47-8P
                                                     188257-52-5P
     188257-53-6DP, solid-supported
                                      188257-54-7P
                                                      188257-55-8P
     188257-56-9DP, solid-supported
                                      221318-06-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction of in the synthesis of achiral amino linker
        reagents for direct labeling of oligonucleotides on solid supports)
IT
     171717-18-3P
                   171717-19-4P
                                  171717-20-7P 171717-21-8P
                                                                 171717-22-9P
                    188366-81-6P
                                   188366-82-7P
     171844-08-9P
                                                                 188366-85-0P
                                                  188366-83-8P
                    188420-41-9P
     188366-86-1P
                                   188420-42-0P
                                                  188420-43-1P
                                                                 188420-44-2P
     222054-01-5P
                    222054-02-6P
                                  222054-03-7P
                                                 222054-04-8P
                                                                 222054-05-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of using achiral amino linker reagents for direct labeling of
        oligonucleotides on solid supports)
     221889-90-3P
IT
     RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of using achiral amino linker reagents in one chain and effect
        on hybridization)
TΤ
     221889-92-5P
                    221889-94-7P
                                   221889-96-9P
                                                  221889-98-1P
                                                                  221890-00-2P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of using achiral amino linker reagents in one chain and effect
        on hybridization)
                3282-30-2, Pivaloyl chloride
IT
     618-88-2
                                               3326-32-7
                                                           28920-43-6,
     9-Fluorenylmethyl chloroformate 35013-72-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of in the synthesis of achiral amino linker reagents for
        direct labeling of oligonucleotides on solid supports)
RE.CNT
        10
              THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L5
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ΑN
     1999:109400 CAPLUS
DN
     130:177546
ΤI
     Methods of receptor modulation and therapeutic and diagnostic uses
     therefor
ΙN
     Morgan, A. Charles, Jr.; Wilbur, D. Scott
PΑ
     Receptagen Corporation, USA; University of Washington
SO
     U.S., 47 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned.
     CODEN: USXXAM
DT
     Patent
LΑ
     English
IC
     ICM A61K031-68
     ICS C12P019-42
NCL 514052000
CC
     1-12 (Pharmacology)
     Section cross-reference(s): 9, 26
```

(Preparation); RACT (Reactant or reagent)

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FAN.CNT 6
     PATENT NO.
                    KIND DATE
                                        APPLICATION NO. DATE
                    ____
                                          -----
PΙ
     US 5869465
                     Α
                           19990209
                                         US 1995-406194
                                                           19950316
     CA 2187346
                     AA 19951019
                                          CA 1995-2187346
                                                           19950407
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PRAI US 1994-224831 B2 19940408
US 1995-406191 A 19950316
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                          19950316
     US 1995-406194 A
                          19950316
     WO 1995-US4404
                     W
                          19950407
     US 1995-545151
                     A3 19951019
     Receptor-modulating agents capable of modulating cell surface receptors by
AΒ
     affecting the cell-surface receptor trafficking pathway are utilized for
     the treatment and diagnosis of a variety of disorders in warm-blooded
     animals, including neoplastic disorders. The receptor-modulating agents
     are comprised of a covalently bound rerouting moiety and targeting moiety.
     Synthesis of several receptor-modulating agents using different functional
     classes of rerouting moieties is described. More specifically, a series
     of examples are presented which employ vitamin B12 as a targeting moiety
     in a receptor-modulating agent.
     receptor modulating agent diagnostic therapeutic; neoplasm diagnosis
ST
     therapy receptor modulating agent; vitamin B12 receptor modulating agent
     prepn
IT
     Protein receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (transcobalamin II; receptor modulation methods, therapeutic and
        diagnostic uses, and receptor-modulating agent prepn.)
IT
     Receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (vitamin B12 and others; receptor modulation methods, therapeutic and
        diagnostic uses, and receptor-modulating agent prepn.)
ΙT
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                  173341-59-8P 189887-10-3P 189887-11-4P
     173341-49-6P
                                                              189887-12-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and reaction; receptor modulation methods, therapeutic and
       diagnostic uses, and receptor-modulating agent prepn.)
IT
     58-85-5, Biotin 60-32-2, 6-Aminocaproic acid 99-31-0
     , 5-Aminoisophthalic acid 99-63-8, Isophthaloyl dichloride 108-30-5,
     Succinic anhydride, reactions 260-94-6D, Acridine, derivs, conjugates
     with cyanocobalamin carboxylic acid diaminododecanesuccinyl deriv.
     769-39-1, 2,3,5,6-Tetrafluorophenol 813-19-4, Bis(tributyltin)
     1711-02-0, 4-Iodobenzoyl chloride 2783-17-7, 1,12-Diaminododecane
     15231-41-1
                 27497-52-5, Tetrafluorophenol
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     173341-35-0
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        (reaction; receptor modulation methods, therapeutic and diagnostic
       uses, and receptor-modulating agent prepn.)
ΙT
     68-19-9D, Vitamin B12, dimers
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(receptor modulation methods, therapeutic and diagnostic uses, and receptor-modulating agent prepn.)
68-19-9, Cyanocobalamin

RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)

(receptor modulation methods, therapeutic and diagnostic uses, and receptor-modulating agent prepn.)

IT 26264-28-8P 38218-55-2P 38218-77-8P 160927-56-0P 173341-26-9P 173341-31-6P

RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)

(receptor modulation methods, therapeutic and diagnostic uses, and receptor-modulating agent prepn.)

IT 72333-39-2P 173341-27-0P 173341-36-1P 173341-37-2P 173341-38-3P 173341-39-4P 173341-40-7DP, conjugate with acridine deriv. 173341-41-8P 173341-42-9P 173341-46-3P 173341-47-4P 173341-48-5P

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(receptor modulation methods, therapeutic and diagnostic uses, and receptor-modulating agent prepn.)

IT 173341-51-0P

IT

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(receptor modulation methods, therapeutic and diagnostic uses, and receptor-modulating agent prepn.)

IT 173341-52-1P 173341-53-2P 173341-54-3P 189887-10-3DP, conjugate with acridine deriv. 189887-11-4DP, conjugate with acridine deriv. 189887-12-5DP, conjugate with acridine deriv.

RL: SPN (Synthetic preparation); PREP (Preparation)

(receptor modulation methods, therapeutic and diagnostic uses, and receptor-modulating agent prepn.)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

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- (2) Anon; EP 0361817 A2 1990 CAPLUS
- (3) Anon; EP 0378203 A2 1990 CAPLUS
- (4) Anon; WO 93/23557 1993 CAPLUS
- (5) Anon; EP 0599325 A1 1994 CAPLUS
- (6) Anon; WO 94/27613 1994 CAPLUS
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- (19) Takahashi, K; Nature 1980, V288(18), P713
- L5 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS AN 1998:776603 CAPLUS

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DN
    130:38642
ΤI
    Preparation of water soluble vitamin B12 as antiinflammatory receptor
    modulating agents
    Morgan, A. Charles, Jr.; Wilbur, D. Scott
IN
PA
    Receptagen Corporation, USA; University of Washington
    U.S., 50 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned.
SO
    CODEN: USXXAM
DT
    Patent
LΑ
    English
    ICM C12P019-42
IC
     ICS A61K031-68
NCL
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     33-7 (Carbohydrates)
     Section cross-reference(s): 1, 34, 63
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                                        CA 1995-2187346 19950407
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    Vitamin B12 antiinflammatory receptor modulating agents capable of
    modulating cell surface receptors by affecting the cell surface receptor
    trafficking pathway are disclosed. The vitamin B12 receptor modulating
     agents are comprised of a covalently bound rerouting moiety and targeting
    moiety linked by a water-solubilizing linker. Synthesis of a vitamin B12/
    biotin conjugate and fusion protein receptor modulating agent is
    reported.
    water soluble linker vitamin B12 prepn; receptor modulating agent vitamin
    B12; vitamin B12 biotin peptide prepn antiinflammatory
ΙT
    Anti-inflammatory agents
        (Prepn. of water sol. vitamin B12 as antiinflammatory receptor
       modulating agents)
IT
    Peptides, preparation
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
    study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic
    use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (Prepn. of water sol. vitamin B12 as antiinflammatory receptor
       modulating agents)
ΙT
    Receptors
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (Prepn. of water sol. vitamin B12 as antiinflammatory receptor
       modulating agents)
ΙT
    12651-28-4, Transcobalamin II
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
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(Prepn. of water sol. vitamin B12 as antiinflammatory receptor modulating agents) IT 56-12-2, GABA, reactions 57-92-1, reactions 58-85-5 68-19-9, Cyanocobalamin **99-31-0** 99-63-8, 1,3-Benzenedicarbonyl dichloride 769-39-1, 2,3,5,6-Tetrafluorophenol 1711-02-0 2783-17-7, 35013-72-0 80366-85-4 86689-14-7 1,12-Dodecanediamine 110079-43-1 173341-32-7 216692-05-6 RL: RCT (Reactant); RACT (Reactant or reagent) (Prepn. of water sol. vitamin B12 as antiinflammatory receptor modulating agents) IT 26264-28-8P 38218-55-2P 38218-77-8P 55729-45-8P 72040-64-3P 160927-56-0P 173341-26-9P 173341-27-0P 173341-31-6P 173341-33-8P 173341-34-9P 173341-35-0P 173341-36-1P 173341-37-2P 173341-38-3P 173341-41-8P 173341-39-4P 173341-40-7P 173341-42-9P 173341-43-0P 173341-44-1P 173341-45-2P 173341-46-3P 173341-47-4P 173341-48-5P 173341-49-6P 173341-51-0P 173341-52-1P 173341-53-2P 173341-54-3P 173341-59-8P 189887-07-8P 189887-08-9P 189887-11-4P 189887-10-3P 189887-12-5P 216757-91-4P 216757-92-5P 216757-93-6P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (Prepn. of water sol. vitamin B12 as antiinflammatory receptor modulating agents) RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD RE (1) Akin, C; Cancer Letters 1993, V69, P51 CAPLUS (2) Anderson, R; Science 1992, V255, P410 CAPLUS (3) Anon; EP 0069450 A1 1983 CAPLUS (4) Anon; EP 0361817 A2 1990 CAPLUS (5) Anon; EP 0378203 A2 1990 CAPLUS (6) Anon; EP 0425680 A1 1991 CAPLUS (7) Anon; WO 93/23557 1993 CAPLUS (8) Anon; EP 0599325 A1 1994 CAPLUS (9) Anon; WO 94/27613 1994 CAPLUS (10) Carpentier, J; Journal of Cellular Physiology 1989, V138, P519 CAPLUS (11) Ciechanover, A; Cell 1994, V79, P13 CAPLUS (12) Gratzer, W; Seminars in Hematology 1993, V30(3), P232 MEDLINE (13) Jabbar, M; Journal of Virology 1990, V64(12), P6297 MEDLINE (14) Joly, M; Science 1994, V263, P684 CAPLUS (15) Krautler, B; Angewandt Chemie International Edition English 1995, V34(1), P84 (16) Kreiner, T; Cell Regulation 1990, V1, P415 CAPLUS (17) Malorni, W; Journal of Cell Science 1993, V106, P309 CAPLUS (18) Mayor, S; Science 1994, V264, P1948 CAPLUS (19) Mayor, S; The Journal of Cell Biology 1993, V121(6), P1257 CAPLUS (20) Parton, R; The Journal of Cell Biology 1994, V127(5), P1199 CAPLUS (21) Pourfarzneh; US 5310656 1994 CAPLUS (22) Robertson, B; Archives of Biochemistry and Biophysics 1992, V292(1), P190 CAPLUS (23) Rodwell; US 5196510 1993 CAPLUS (24) Ross, J; Cancer 1994, V73(9), P2432 CAPLUS (25) Russel-Jones; US 5428023 1995 CAPLUS (26) Schnitzer, J; The Journal of Cell Biology 1994, V127(5), P1217 CAPLUS (27) Selhub; US 4167556 1979 CAPLUS (28) Sigal, N; Annual Review Immunology 1992, V10, P519 CAPLUS (29) Takahashi, K; Nature 1980, V288(18), P713 (30) Thiele, D; Transplantation 1992, V53(6), P1334 MEDLINE

L5 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS

AN 1998:776598 CAPLUS

DN 130:38641

TI Preparation of water soluble vitamin B12 as antiinflammatory receptor modulating agents

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PA
    Receptagen Corporation, USA; University of Washington
SO
     U.S., 66 pp., Cont.-in-part of U.S. Ser. No. 406,191.
     CODEN: USXXAM
DT
    Patent
    English
LA
IC
    ICM A01N043-04
     ICS A61K031-70
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    514052000
CC
     33-7 (Carbohydrates)
     Section cross-reference(s): 1, 34, 63
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    US 5840712
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    Vitamin B12 antiinflammatory receptor modulating agents capable of
AB
    modulating cell surface receptors by affecting the cell surface receptor
    trafficking pathway are disclosed. The vitamin B12 receptor modulating
    agents are comprised of a covalently bound rerouting moiety and targeting
    moiety linked by a water-solubilizing linker. Synthesis of a vitamin B12/
    biotin conjugate and fusion protein receptor modulating agent is
    reported.
ST
    water soluble linker vitamin B12 prepn; receptor modulating agent vitamin
    B12; vitamin B12 biotin peptide prepn antiinflammatory
IT
    Anti-inflammatory agents
        (prepn. of water sol. vitamin B12 as antiinflammatory receptor
       modulating agents)
IT
    Peptides, preparation
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
    study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic
    use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of water sol. vitamin B12 as antiinflammatory receptor
       modulating agents)
IT
    Receptors
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
    (Biological study); PROC (Process)
        (prepn. of water sol. vitamin B12 as antiinflammatory receptor
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Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.

IN

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modulating agents)
IT
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        (prepn. of water sol. vitamin B12 as antiinflammatory receptor
        modulating agents)
IT
     12651-28-4, Transcobalamin II
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
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     4-Iodobenzoyl chloride
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     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of water sol. vitamin B12 as antiinflammatory receptor
       modulating agents)
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        (prepn. of water sol. vitamin B12 as antiinflammatory receptor
       modulating agents)
RE.CNT
              THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
RF.
(1) Akin, C; Cancer Letters 1993, V69, P51 CAPLUS
(2) Anderson, R; Science 1992, V255(24), P410
(3) Anon; EP 0069450 A1 1983 CAPLUS
(4) Anon; EP 0361817 A2 1990 CAPLUS
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- (31) Russell-Jones; US 5548064 1996 CAPLUS
- (32) Russell-Jones; US 5589463 1996 CAPLUS
- (33) Selhub; US 4167556 1979 CAPLUS
- (34) Takahashi, K; Nature 1980, V288(18), P713
- L5 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS
- AN 1998:236288 CAPLUS
- DN 128:295003
- TI Preparation of biotinylated cobalamins as antiinflammatory agents and transcobalamin II receptors
- IN Wilbur, D. Scott; Pathare, Pradip M.; Morgan, A. Charles, Jr.
- PA University of Washington, USA; Receptagen Corp.
- SO U.S., 58 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned. CODEN: USXXAM
- DT Patent
- LA English
- IC ICM A61K031-70
  - ICS A61K038-16; C07H023-00; C07K001-113
- NCL 530367000
- CC 33-7 (Carbohydrates)
  - Section cross-reference(s): 1, 63

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		5840712				20021015				JP 1995-526497 AT 1995-916284								
	US			Α					US 1995-545151			19951019						
PRAI								US	US 1998-200422									
	US	1995-406	А		1995													
		3 1995-406192 3 1995-406194		A A		1995 1995												
		O 1995-US4404				1995												
	US	1995-545	151	A3	3	1995	1019											

AB A biotinylated cobalamin, formed from a vitamin B12 mol. coupled to a biotin mol., is disclosed. In a preferred embodiment, the vitamin B12 mol. is cyanocobalamin. The biotin mol. can also be coupled to a rerouting moiety, optionally through a biotin binding protein such as avidin or streptavidin. The biotinylated cobalamin binds to a cell surface receptor, is invaginated, and once internalized affects the receptor trafficking pathway.

ST biotinylated cyanocobalamin prepn antiinflammatory transcobalamin receptor IT Anti-inflammatory agents

(prepn. of biotinylated cobalamins as antiinflammatory agents and transcobalamin II receptors)

IT Receptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

```
(prepn. of biotinylated cobalamins as antiinflammatory agents and
         transcobalamin II receptors)
IT
      160927-56-0P
                    173341-26-9P
                                  173341-27-0P
                                                   173341-31-6P
      RL: BAC (Biological activity or effector, except adverse); BSU (Biological
      study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
      (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
      (Reactant or reagent); USES (Uses)
         (prepn. of biotinylated cobalamins as antiinflammatory agents and
         transcobalamin II receptors)
 IT
      50479-22-6
      RL: BAC (Biological activity or effector, except adverse); BSU (Biological
      study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL
      (Biological study); RACT (Reactant or reagent); USES (Uses)
         (prepn. of biotinylated cobalamins as antiinflammatory agents and
         transcobalamin II receptors)
 IT
      173341-36-1P
                    173341-37-2P
                                   173341-38-3P
                                                   173341-39-4P 173341-40-7P
      173341-41-8P
                    173341-42-9P
                                    173341-46-3P
                                                   173341-47-4P
                                                                  173341-48-5P
     189887-08-9P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
      BIOL (Biological study); PREP (Preparation); USES (Uses)
         (prepn. of biotinylated cobalamins as antiinflammatory agents and
         transcobalamin II receptors)
 IT
     12651-28-4, Transcobalamin II
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
      (Biological study); PROC (Process)
         (prepn. of biotinylated cobalamins as antiinflammatory agents and
         transcobalamin II receptors)
 IT
     58-85-5, Biotin
                       60-32-2, 6-Aminocaproic acid
                                                       68-19-9.
     Cyanocobalamin 99-31-0, 5-Aminoisophthalic acid
     2,3,5,6-Tetrafluorophenol 2783-17-7, 1,12-Diaminododecane
     RL: RCT (Reactant); RACT (Reactant or reagent)
         (prepn. of biotinylated cobalamins as antiinflammatory agents and
         transcobalamin II receptors)
 ΙT
     26264-28-8P
                   38218-55-2P
                                  38218-77-8P
                                               55729-45-8P
                                                              72040-64-3P
     173341-33-8P
                   173341-34-9P
                                    173341-35-0P
                                                 173341-49-6P
                                                                  173341-59-8P
     189887-10-3P
                    189887-11-4P
                                    189887-12-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (prepn. of biotinylated cobalamins as antiinflammatory agents and
         transcobalamin II receptors)
ΙT
     173341-32-7P
                    173341-43-0P
                                   173341-44-1P
                                                   173341-45-2P
                                                                  173341-51-0P
     173341-52-1P
                    173341-53-2P
                                   173341-54-3P
                                                   189887-07-8P
     RL: SPN (Synthetic preparation); PREP (Preparation)
         (prepn. of biotinylated cobalamins as antiinflammatory agents and
        transcobalamin II receptors)
L5
     ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS
AN
     1997:377886 CAPLUS
DN
     126:343813
TΙ
     Preparation of vitamin B12 receptor modulating agents
IN
     Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
     Receptagen Corporation, USA; University of Washington; Morgan, A. Charles,
PΑ
     Jr.; Wilbur, D. Scott; Pathare, Pradip, M.
SO
     PCT Int. Appl., 97 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM C07H023-00
CC
     33-9 (Carbohydrates)
FAN.CNT 6
     PATENT NO.
                      KIND DATE
                                          APPLICATION NO. DATE
```

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ΡI
     WO 9714711
                       A1
                            19970424
                                            WO 1996-US16672 19961018
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG
     US 5840712
                            19981124
                                           US 1995-545151
                       Α
                                                             19951019
     AU 9677182
                       Α1
                            19970507
                                            AU 1996-77182
                                                             19961018
     EP 1015475
                       Α1
                            20000705
                                            EP 1996-940247
                                                             19961018
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
PRAI US 1995-545151
                       Α
                            19951019
     US 1995-545496
                       Α
                            19951019
     US 1994-224831
                       В2
                            19940408
     US 1995-406191
                       A2
                            19950316
     US 1995-406192
                       Α2
                            19950316
     US 1995-406194
                       A2
                            19950316
     WO 1996-US16672
                       W
                            19961018
OS
     MARPAT 126:343813
AΒ
     Vitamin B12 receptor modulating agents capable of modulating cell surface
     receptors by affecting the cell surface receptor trafficking pathway are
     disclosed. The vitamin B12 receptor modulating agents are comprised of a
     covalently bound rerouting moiety and targeting moiety linked by a
     water-solubilizing linker.
ST
     receptor modulating agent vitamin B12 prepn; nucleoside vitamin B12 prepn
     antiinflammatory; vitamin B12 prepn receptor antiinflammatory
IT
     Anti-inflammatory agents
        (prepn. and antiinflammatory activity of vitamin B12 receptor
        modulating agents)
IT
     Receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (vitamin B12 modulating agents; prepn. and antiinflammatory activity of
        vitamin B12 receptor modulating agents)
IT
     Nucleosides, preparation
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (vitamin B12; prepn. and antiinflammatory activity of vitamin B12
        receptor modulating agents)
IT
     189887-08-9P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (prepn. and antiinflammatory activity of vitamin B12 receptor
        modulating agents)
IT
     173341-40-7P
                    173341-41-8P
                                  173341-42-9P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. and antiinflammatory activity of vitamin B12 receptor
        modulating agents)
IT
     57-92-1, Streptomycin, reactions
                                        58-85-5, Biotin
                                                           60 - 32 - 2,
     6-Aminocaproic acid 68-19-9, Vitamin B12
                                                 86-38-4 99-31-0,
     5-AminoisophthALIC ACID
                               99-63-8, 1,3-Benzenedicarbonyl dichloride
     769-39-1, 2,3,5,6-TETRAFLUOROPHENOL
                                           1711-02-0, 4-Iodobenzoyl chloride
     4246-51-9
                 38218-77-8
                              50479-22-6
                                           173341-33-8
                                                          173341-35-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
```

```
(prepn. and antiinflammatory activity of vitamin B12 receptor
        modulating agents)
IT
     68-19-9DP, Cyanocobalamin, b, d, or e-diaminododecanamide acridine or
     biotinylated isophthaloyl derivs. 2783-17-7P, 1,12-Diaminododecane
                   38218-55-2P 72040-64-3P 160927-56-0P 173341-26-9P
     26264-28-8P
     173341-27-0P
                    173341-31-6P
                                    173341-32-7P
                                                   173341-34-9P
                                                                   173341-36-1P
     173341-37-2P
                    173341-38-3P
                                    173341-39-4P
                                                   173341-46-3P
                                                                   173341-47-4P
     173341-48-5P
                    173341-49-6P
                                    173341-59-8P
                                                   189887-07-8P
                                                                   189887-10-3P
     189887-11-4P
                    189887-12-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. and antiinflammatory activity of vitamin B12 receptor
        modulating agents)
     173341-51-0P
IT
                    173341-52-1P
                                    173341-53-2P
                                                   173341-54-3P
                                                                   188014-58-6P
     188014-60-0P
                    189887-13-6P
                                    189887-14-7P
                                                   189887-15-8P
                                                                   189887-16-9P
     189887-17-0P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. and antiinflammatory activity of vitamin B12 receptor
        modulating agents)
L5
     ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS
ΑN
     1997:251007 CAPLUS
DN
     126:238622
TΙ
     A new achiral linker reagent for the incorporation of multiple amino
     groups into oligonucleotides
ΙN
     Behrens, Carsten; Petersen, Kenneth H.; Egholm, Michael; Nielsen, John;
     Dahl, Otto
     Behrens, Carsten, Den.; Petersen, Kenneth H.; Egholm, Michael; Nielsen,
PA
     John; Dahl, Otto
SO
     PCT Int. Appl., 34 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM C07H021-00
     ICS C07F009-24; C07F009-141; C12Q001-68; G01N033-543
CC
     33-10 (Carbohydrates)
FAN.CNT 1
     PATENT NO.
                      KIND DATE
                                           APPLICATION NO.
                                                             DATE
     _____
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                            _____
                                            -----
PΙ
     WO 9705156
                      A1 19970213
                                          WO 1996-DK330
                                                             19960726
            AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ,
             DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE,
             KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT
     AU 9665140
                      A1
                            19970226
                                           AU 1996-65140
                                                             19960726
PRAI DK 1995-863
                            19950727
     WO 1996-DK330
                            19960726
OS
     MARPAT 126:238622
GΙ
R^{3}O(CH_{2})_{n}
                (CH<sub>2</sub>)<sub>n</sub>OR<sup>1</sup>
            ZNHR<sup>2</sup>
                            Ι
```

AB Functionalized achiral linker reagents, e.g. I [n = 1-3; Z = bond, C1-C10]

chain optionally interrupted by 1-5 heteroatoms; R1 = H-phosphonate, phosphoramidite; R2 = amino protecting groups, e.g., PhCH2O2C, Me3CO2C, 9-fluorenylmethoxycarbonyl, allyloxycarbonyl, F3CCO, phthaloyl and reporter groups, e.g., fluorescein, dansyl, biotin, digoxigenin, N-oxyl-4, 4-dimethyloxazolidine, N-oxyl-2, 2, 5, 5-tetramethylpyrrolidine, texas red, tetramethylrhodamine, etc.; R3 = H, hydroxy protecting group, e.g., 4,4'-dimethoxytrityl, 9-fluorenylmethoxycarbonyl, etc.] were prepd. and used to incorporate multiple primary amino groups or reporter groups into oligodeoxyribonucleotides following the phosphoramidite methodol. is possible to substitute any deoxyribonucleotide, deoxynucleotide, or nucleotide with the linker in conventional phosphoramidite or H-phosphonate DNA syntheses. Thus, the bis(hydroxymethyl)benzylamine I (Z = CH2; R1 = H; R2 = 9-fluorenylmethylcarbonyl; R3 = 4,4'-dimethoxytrityl; n = 1) was prepd. from 5-nitroisophthalic acid in seven steps. Application of this reagent in std. solid-support phosphoramidite oligodeoxyribonucleotide prepn. methodol. gave, e.g., 5'-GTAGATCACT-P(O)(OH)OCH2-X-CH2OH-3' [X = 1,3-(5-H2NCH2)C6H3] with 99.5% coupling efficiency. achiral linker oligodeoxyribonucleotide solid phase prepn; amino group incorporation oligodeoxyribonucleotide prepn; aminomethylbenzenedimethanol linker oligodeoxyribonucleotide prepn Solid phase synthesis (prepn. of bis(hydroxymethyl)benzylamine achiral linker reagents for oligodeoxyribonucleotide solid phase prepn.) Oligodeoxyribonucleotides RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of bis(hydroxymethyl)benzylamine achiral linker reagents for oligodeoxyribonucleotide solid phase prepn.) 108-67-8, Mesitylene, reactions 610-27-5, 5-Nitrophthalic acid 1074-82-4, Potassium phthalimide 27072-45-3, Fluorescein isothiocyanate 28920-43-6, 9-Fluorenylmethyl chloroformate 35013-72-0 102691-36-1, 2-Cyanoethyl N, N, N', N'-tetraisopropylphosphorodiamidite RL: RCT (Reactant); RACT (Reactant or reagent) (prepn. of bis(hydroxymethyl)benzylamine achiral linker reagents for oligodeoxyribonucleotide solid phase prepn.) **99-31-0P**, 5-Aminoisophthalic acid 27129-86-8P, 3,5-Dimethylbenzyl bromide 42122-73-6P 71176-54-0P, 5-Amino-1,3-benzenedimethanol 146335-23-1P 171082-06-7P 171082-07-8P 171082-08-9DP, LCAA-CPG polymer support 171082-09-0P 188257-47-8P 188257-48-9P 188257-49-0P 188257-50-3P 188257-51-4P 188257-52-5P 188257-53-6DP, LCAA-CPG polymer support 188257-54-7P 188257-55-8P 188257-56-9DP, LCAA-CPG polymer support RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of bis(hydroxymethyl)benzylamine achiral linker reagents for oligodeoxyribonucleotide solid phase prepn.) 171717-18-3P 171717-19-4P 171717-20-7P 171717-21-8P 171717-22-9P 171844-08-9P 188366-81-6P 188366-82-7P 188366-83-8P 188366-85-0P 188366-86-1P 188420-41**-**9P 188420-42-0P 188420-43-1P 188420-44-2P RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of bis(hydroxymethyl)benzylamine achiral linker reagents for oligodeoxyribonucleotide solid phase prepn.) ANSWER 14 OF 15 CAPLUS COPYRIGHT 2003 ACS 1997:155067 CAPLUS 126:207193 Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin Ring Carboxylates and Evaluation of Their Binding to Transcobalamin. 2 Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon;

Quadros, Edward V.; McLoughlin, Patricia; Morgan, A. Charles

Department of Radiation Oncology, University of Washington, Seattle, WA,

ST

ΙT

ΙT

ΙT

ΙT

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L5

ΑN

DN

ΤI

ΑU

CS

98195, USA SO Bioconjugate Chemistry (1997), 8(2), 161-172 CODEN: BCCHES; ISSN: 1043-1802 American Chemical Society DTJournal LΑ English CC 1-6 (Pharmacology) Section cross-reference(s): 78 AΒ Several cobalamin (Cbl) dimers have been prepd. for evaluation as potential antiproliferative agents in the treatment of AIDS-related lymphoma. The Cbl dimers were synthesized by crosslinking Cbl carboxylates, produced by acid hydrolysis of the b-, d-, and e-propionamide side chains of cyanocobalamin (CN-Cbl), through an isophthalate mol. Linking mols. were used between the Cbl carboxylates and the isophthalate moiety. The linkers were incorporated to provide a distance between the two Cbl mols. such that the dimeric Cbls might bind two mols. of transcobalamin II (TCII), the Cbl transport protein in plasma. Initially, the linking moiety used was 1,12-diaminododecane, but the resulting dimers had low ag. soly. To improve the soly. of the dimers, 4,7,10-trioxa-1,13-tridecanediamine was employed as the linking moiety. This improved the water soly. of the dimers considerably, while retaining the distance between the Cbl mols. at 41-42 .ANG. (fully extended). To introduce addnl. substitution on Cbl dimers, 5-aminoisophthalic acid was used as the crosslinking reagent. P-Iodobenzoyl and p-(tri-n-butylstannyl)benzoyl conjugates of 5-aminoisophthalate were synthesized and used to prep. Cbl dimers. The stannylbenzoyl-conjugated Cbl dimers were prepd. as precursors to be used in radioiodination reactions, and the iodobenzoyl-conjugated Cbl dimers were prepd. as HPLC stds. for the radioiodinated product. Attempts to iodinate/radioiodinate the stannylbenzoyl Cbl dimers were unsuccessful. Although an explanation for this is not readily apparent, the failure to react may be due to the lipophilicity of the linker used and the steric environment of the two Cbl moieties. A biotinylated deriv. of 5-aminoisophthalate was also synthesized and used to prep. biotinylated-Cbl dimers. In a competitive rhTCII binding assay with [57Co]CN-Cbl, Cbl dimers contg. the lipophilic diaminododecane linking moiety had decreased binding avidities compared to those of Cbl monomers substituted at the same corrin ring carboxylate. However, Cbl dimers contg. the water-solubilizing trioxadiamine linker appeared to have avidities similar to those of the Cbl monomers. ST cobalamin dimer prepn transcobalamin binding ΙT 173341-40-7P 173341-41-8P 173341-42-9P 173341-43-0P 173341-44-1P 173341-46-3P 173341-47-4P 173341-48-5P 173341-52-1P 173341-53-2P 173341-54-3P 188014-66-6P 188014-67-7P 188014-68-8P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. of cobalamin dimers and binding to human recombinant transcobalamin II) ΙT 12651-28-4, Transcobalamin II RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (prepn. of cobalamin dimers and binding to human recombinant transcobalamin II) 68-19-9P, Cyanocobalamin ΙT RL: PUR (Purification or recovery); PREP (Preparation) (prepn. of cobalamin dimers and binding to human recombinant transcobalamin II) ΙT 58-85-5P, **Biotin 99-31-0P** 26264-28-8P 38218-55-2P 38218-77-8P 160927-56-0P 173341-26-9P 173341-31-6P 173341-49-6P 173341-51-0P 173341-59-8P 188014-58-6P 188014-59-7P 188014-60-0P

188014-61-1P 188014-62-2P 188014-63-3P 188014-64-4P 188014-65-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of cobalamin dimers and binding to human recombinant transcobalamin II)

- L5 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2003 ACS
- AN 1991:225167 CAPLUS
- DN 114:225167
- TI Method of assaying substances and immunoassay element employing .beta.-D-galactosidase
- IN Onishi, Akira; Kawakatsu, Satoshi; Ito, Tsukasa; Takahashi, Takenori; Fukaya, Michie
- PA Konica Co., Japan
- SO Eur. Pat. Appl., 61 pp.
  - CODEN: EPXXDW
- DT Patent
- LA English
- IC ICM G01N033-58
  - ICS G01N033-543; G01N033-52
- CC 9-1 (Biochemical Methods)
  - Section cross-reference(s): 15

## FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE						
PI	EP 328106	A2	19890816	EP 1989-102245	19890209						
	EP 328106	<b>A</b> 3	19901219								
	R: DE, GB										
	JP 01308966	A2	19891213	JP 1989-31530	19890209						
	JP 01308967	A2	19891213	JP 1989-31531	19890209						
PRAI	JP 1988-29632		19880209								
	JP 1988-29633		19880209								

OS MARPAT 114:225167

Disclosed is an assay element and a method of assaying a target substance in a fluid sample. In this method, a) the target substance; b) a substance which specifically binds to the target substance, to which a biol. active substance which does not bind to the target substance is attached, or to which a substance which specifically binds to a biol. active substance which does not bind to the target substance is attached; c) a labeled substance which is the target substance or an analog thereof labeled with .beta.-D-galactosidase, or which is a substance which specifically binds to the target substance, labeled with .beta.-D-galactosidase; d) a substance which specifically binds to the biol. active substance and which does not bind to the target substance, or the biol. active substance, which is fixed to a carrier, which carrier exists in a porous reaction layer of an assay element; and e) a substance which specifically binds to .beta.-D-galactosidase and which changes a signal originated from .beta.-D-galactosidase, which is fixed to said carrier or another carrier which exists in a porous reaction layer of an assay element, are reacted, and the change of the signal from .beta.-D-galactosidase is measured. Human IgG was detd. by mixing the sample with bis(2-hydroxyethyl)iminotris(hydroxymethyl)methane, .beta.-D-galactosidase-labeled human IgG, and biotin-bound anti-human IgG antibody and applying the mixt. to an immunoassay element comprising a PET film coated with 1) a soln. contg. gelatin, Triton X-100, 1,2-bis(vinylsulfonyl)ethane, and H2O; 2) a soln. contg. p-aminophenylmercuric acetate-bound Avicel (microcryst. cellulose), Triton X-100, polyvinylpyrrolidone, 5-bromo-4-chloro-3-indolyl-.beta.-Dgalactopyranoside, 3,3'-(4,4'-biphenylene)-bis(2,5-diphenyl-2H-tetrazolium chloride), and n-BuOH; 3) a soln. contg. avidin-bound Avicel contg. bovine serum albumin and sucrose, Triton X-100, polyvinylpyrrolidone, and n-BuOH; and 4) a soln. contg. cellulose powder D, Triton X-100, polyvinylpyrrolidone, and n-BuOH. The element was incubated at 37.degree.

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for 10 min and then the reflection d. at 546 nm was measured from the side
     of the support layer.
ST
     galactosidase immunoassay test strip; human IgG detn galactosidase
     immunoassay
IT
     Blood analysis
        (IgG of human detn. in, by .beta.-D-galactosidase immunoassay)
IT
     Antibodies
     Antigens
     Avidins
     RL: ANST (Analytical study)
        (in .beta.-D-galactosidase immunoassays)
IΤ
     Escherichia coli
        (.beta.-D-galactosidase of, in immunoassay)
     Immunoglobulins
IT
     RL: ANST (Analytical study)
        (G, detn. of human, by .beta.-D-galactosidase immunoassay test strip)
ΙT
     Immunoglobulins
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (G, reaction products, with .beta.-D-galactosidase, prepn. of, for
        human IqG detn. by .beta.-D-galactosidase immunoassay)
ΙT
     Analysis
        (biochem., by specific binding assay using .beta.-D-galactosidase as
     Spectrochemical analysis
ΙT
        (fluorometric, by specific binding assay using .beta.-D-galactosidase
        as label)
ΙT
     Immunochemical analysis
        (immunoassay, .beta.-D-galactosidase as label in)
IT
     Immunochemical analysis
        (immunoassay, app., carriers for, using galactosidase label)
IT
     Avidins
     RL: ANST (Analytical study)
        (reaction products, with cellulose, .beta.-D-galactosidase immunoassay
        test strip contg., for human IgG detn.)
IT
     Spectrochemical analysis
        (spectrophotometric, by specific binding assay using
        .beta.-D-galactosidase as label)
IT
     Onium compounds
     RL: ANST (Analytical study)
        (tetrazolium, salts, in .beta.-D-galactosidase immunoassays)
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     369-07-3, o-Nitrophenyl-.beta.-D-galactopyranoside
     RL: ANST (Analytical study)
        (IgG of human detn. by .beta.-D-galactosidase immunoassay test strip
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ΙT
     369-07-3
               1158-17-4 2818-58-8
                                      7240-90-6
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     17817-20-8
                  33993-25-8 55508-29-7 78261-89-9 87810-64-8
     97753-82-7
                 99792-79-7D, derivs.
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     126787-65-3D, derivs.
     RL: ANST (Analytical study)
        (as enzyme substrate in .beta.-D-galactosidase immunoassays)
IT
     9031-11-2D, conjugates
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        (in immunoassays)
IT
     58-85-5, Biotin
                     5625-37-6, Piperazine-N, N'-bis(2-
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                           6976-37-0
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     compds. 7440-22-4D, Silver, organo compds.
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     p-Aminophenyl-.beta.-D-thiogalactopyranoside
                                                    107537-94-0, Galactostatin
     RL: ANST (Analytical study)
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ΙT
    9001-46-1DP, Glutamic acid dehydrogenase, anti-human IgG antibody reaction
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    RL: SPN (Synthetic preparation); PREP (Preparation)
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     58-85-5DP, Biotin, anti-human IgG antibody reaction products
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     99-31-ODP, 5-Aminoisophthalic acid, Avicel reaction products
     6283-24-5DP, p-Aminophenyl mercuric acetate, cellulose reaction products
     9004-34-6DP, Cellulose, p-aminophenyl mercuric acetate reaction products
     16758-34-2DP, Avicel reaction products
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        (prepn. of, for human IgG detn. by .beta.-D-galactosidase immunoassay)
     9004-34-6, Avicel, reactions
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L5
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E3
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AN
     2002:319261 CAPLUS
     137:59601
DN
ΤI
    A Streptavidin-Biotin Binding System That Minimizes Blocking by Endogenous
     Biotin
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ΑU
     Hamblett, Kevin J.; Kegley, Brian B.; Hamlin, Don K.; Chyan, Ming-Kuan;
     Hyre, David E.; Press, Oliver W.; Wilbur, D. Scott; Stayton, Patrick S.
CS
     Departments of Bioengineering, Medicine, and Radiation Oncology,
     University of Washington, Seattle, WA, 98195, USA
     Bioconjugate Chemistry (2002), 13(3), 588-598
SO
     CODEN: BCCHES; ISSN: 1043-1802
PB
     American Chemical Society
DT
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LΑ
     English
RE.CNT 41
              THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L7
     ANSWER 2 OF 17 CAPLUS COPYRIGHT 2003 ACS
AN
     2001:137180 CAPLUS
     134:178346
DN
TΙ
     Preparation of novel naphthalenesulfonic acids and related compounds,
     method of preparation and use as glucose uptake agonists
IN
     Spevak, Wayne R.; Shi, Songyuan; Prasad, V. V. S. V. Manchem; Kozlowski,
     Michael R.; Schow, Steven R.; Lum, Robert T.; Robinson, Louise; Park,
     Jeong Weong
PA
     Telik, Inc., USA
SO
     PCT Int. Appl., 94 pp.
     CODEN: PIXXD2
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AN
     2000:35037 CAPLUS
DN
     132:90367
     Trifunctional reagent for conjugation to a biomolecule for use in
ΤI
     diagnosis and therapy
     Wilbur, D. Scott; Sandberg, Bengt E. B.
IN
PA
     Dept. of Radiation Oncology, University of Washington, USA; Mitra Medical
     Technology AB
SO
     PCT Int. Appl., 48 pp.
     CODEN: PIXXD2
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AN
     2000:35036 CAPLUS
DN
     132:90366
TI
     Trifunctional reagent for conjugation to a biomolecule for use in
     diagnosis and therapy
     Wilbur, D. Scott; Sandberg, Bengt E. B.
ΙN
     Department of Radiation Oncology, University of Washington, USA; Mitra
PA
     Medical Technology AB
SO
     PCT Int. Appl., 41 pp.
     CODEN: PIXXD2
DT
     Patent
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     English
FAN.CNT 2
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L7
     ANSWER 5 OF 17 CAPLUS COPYRIGHT 2003 ACS
ΑN
     1999:668186 CAPLUS
     132:46430
DN
     Molecular Necklaces. Cross-Linking Hemoglobin with Reagents Containing
TI
     Covalently Attached Ligands
     Crapatureanu, Sanda; Serbanescu, Ruxandra; Brevitt, Sharon Bisley; Kluger,
ΑU
     Ronald
CS
     Lash Miller Laboratories Department of Chemistry, University of Toronto,
     Toronto, ON, M5S 3H6, Can.
     Bioconjugate Chemistry (1999), 10(6), 1058-1067
     CODEN: BCCHES; ISSN: 1043-1802
PΒ
     American Chemical Society
DΤ
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     English
LΑ
OS
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     1999:140535 CAPLUS
AN
DN
     130:267698
ΤI
     Synthesis of achiral linker reagents for direct labeling of
     oligonucleotides on solid supports
ΑU
     Behrens, Carsten; Dahl, Otto
CS
     Department of Chemistry, University of Copenhagen, Copenhagen, DK-2100,
     Den.
SO
     Nucleosides & Nucleotides (1999), 18(2), 291-305
     CODEN: NUNUD5; ISSN: 0732-8311
PΒ
     Marcel Dekker, Inc.
DΤ
     Journal
     English
RE.CNT 10
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- L7 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2003 ACS
- AN 1998:776603 CAPLUS
- DN 130:38642
- TI Preparation of water soluble vitamin B12 as antiinflammatory receptor modulating agents

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Morgan, A. Charles, Jr.; Wilbur, D. Scott
ΙN
    Receptagen Corporation, USA; University of Washington
PΑ
    U.S., 50 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned.
SO
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    ANSWER 8 OF 17 CAPLUS COPYRIGHT 2003 ACS
    1998:776598 CAPLUS
ΑN
ĎΝ
    130:38641
     Preparation of water soluble vitamin B12 as antiinflammatory receptor
ΤI
    modulating agents
IN
    Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
    Receptagen Corporation, USA; University of Washington
    U.S., 66 pp., Cont.-in-part of U.S. Ser. No. 406,191.
    CODEN: USXXAM
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     ANSWER 9 OF 17 CAPLUS COPYRIGHT 2003 ACS
L7
AN
     1997:594715 CAPLUS
DN
     127:262560
ΤI
     Synthetic derivatives of rapamycin as multimerizing agents for chimeric
     proteins with immunophilin derived domains
     Holt, Dennis A.; Keenan, Terence P.; Guo, Tao; Laborde, Edgardo; Yang, Wu
IN
PΑ
     Ariad Gene Therapeutics, Inc., USA; Holt, Dennis A.; Keenan, Terence P.;
     Guo, Tao; Laborde, Edgardo; Yang, Wu
SO
     PCT Int. Appl., 98 pp.
     CODEN: PIXXD2
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     Patent
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LA
FAN.CNT 3
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    Synthetic derivatives of rapamycin as multimerizing agents for chimeric
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    Holt, Dennis A.; Keenan, Terence P.; Guo, Tao; Laborde, Edgardo; Yang, Wu
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    Ariad Gene Therapeutics, Inc., USA; Holt, Dennis A.; Keenan, Terence P.;
    Guo, Tao; Laborde, Edgardo; Yang, Wu
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     Preparation of vitamin B12 receptor modulating agents
IN
     Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
PA
     Receptagen Corporation, USA; University of Washington; Morgan, A. Charles,
     Jr.; Wilbur, D. Scott; Pathare, Pradip, M.
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    A new achiral linker reagent for the incorporation of multiple
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     Behrens, Carsten; Petersen, Kenneth H.; Egholm, Michael; Nielsen, John;
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     Behrens, Carsten, Den.; Petersen, Kenneth H.; Egholm, Michael; Nielsen,
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     Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin
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     Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon;
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CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
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     Catalytic antibodies for activation of carbamate-containing prodrugs and
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     Blackburn, George Michael; Wentworth, Paul
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    Preparation of vitamin B12 derivatives as receptor modulating agents for
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IN
    Morgan, A. Charles; Wilbur, D. Scott; Pathare, Pradip M.
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    A new achiral reagent for the incorporation of multiple amino groups into
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    Bioorganic & Medicinal Chemistry Letters (1995), 5(16), 1785-90
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     Hamblett, Kevin J.; Kegley, Brian B.; Hamlin, Don K.; Chyan, Ming-Kuan;
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CS
     Departments of Bioengineering, Medicine, and Radiation Oncology,
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     Trifunctional reagent for conjugation to a biomolecule for use in
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     Wilbur, D. Scott; Sandberg, Bengt E. B.
PA
     Dept. of Radiation Oncology, University of Washington, USA; Mitra Medical
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SO
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     Wilbur, D. Scott; Sandberg, Bengt E. B.
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     Department of Radiation Oncology, University of Washington, USA; Mitra
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     1999:668186 CAPLUS
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     132:46430
     Molecular Necklaces. Cross-Linking Hemoglobin with Reagents Containing
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     Crapatureanu, Sanda; Serbanescu, Ruxandra; Brevitt, Sharon Bisley; Kluger,
ΑU
     Ronald
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Lash Miller Laboratories Department of Chemistry, University of Toronto,

CS

Toronto, ON, M5S 3H6, Can.

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AN
     1999:140535 CAPLUS
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     Synthesis of achiral linker reagents for direct labeling of
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ΑU
     Behrens, Carsten; Dahl, Otto
CS
     Department of Chemistry, University of Copenhagen, Copenhagen, DK-2100,
     Den.
     Nucleosides & Nucleotides (1999), 18(2), 291-305
SO
     CODEN: NUNUD5; ISSN: 0732-8311
PB
     Marcel Dekker, Inc.
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     ANSWER 6 OF 10 CAPLUS COPYRIGHT 2003 ACS
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     130:38642
DN
     Preparation of water soluble vitamin B12 as antiinflammatory receptor
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     modulating agents
IN
     Morgan, A. Charles, Jr.; Wilbur, D. Scott
PA
     Receptagen Corporation, USA; University of Washington
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     U.S., 50 pp., Cont.-in-part of U.S. Ser. No. 224,831, abandoned.
     CODEN: USXXAM
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     130:38641
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     Preparation of water soluble vitamin B12 as antiinflammatory receptor
     modulating agents
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     Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
     Receptagen Corporation, USA; University of Washington
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     U.S., 66 pp., Cont.-in-part of U.S. Ser. No. 406,191.
     CODEN: USXXAM
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    1997:377886 CAPLUS
DN
    126:343813
    Preparation of vitamin B12 receptor modulating agents
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IN
    Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
    Receptagen Corporation, USA; University of Washington; Morgan, A. Charles,
PA
    Jr.; Wilbur, D. Scott; Pathare, Pradip, M.
    PCT Int. Appl., 97 pp.
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ΤI
     A new achiral linker reagent for the incorporation of multiple
     amino groups into oligonucleotides
IN
     Behrens, Carsten; Petersen, Kenneth H.; Egholm, Michael; Nielsen, John;
     Dahl, Otto
     Behrens, Carsten, Den.; Petersen, Kenneth H.; Eqholm, Michael; Nielsen,
PA
     John; Dahl, Otto
SO
     PCT Int. Appl., 34 pp.
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     1997:155067 CAPLUS
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     126:207193
     Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin
TI
     Ring Carboxylates and Evaluation of Their Binding to Transcobalamin. 2
ΑU
     Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon;
     Quadros, Edward V.; McLoughlin, Patricia; Morgan, A. Charles
CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
SO
     Bioconjugate Chemistry (1997), 8(2), 161-172
     CODEN: BCCHES; ISSN: 1043-1802
     American Chemical Society
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     134:178346
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     Preparation of novel naphthalenesulfonic acids and related compounds,
     method of preparation and use as glucose uptake agonists
     Spevak, Wayne R.; Shi, Songyuan; Prasad, V. V. S. V. Manchem; Kozlowski,
IN
     Michael R.; Schow, Steven R.; Lum, Robert T.; Robinson, Louise; Park,
     Jeong Weong
     Telik, Inc., USA
PΑ
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ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS

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DN
     127:262560
ΤI
     Synthetic derivatives of rapamycin as multimerizing agents for chimeric
     proteins with immunophilin derived domains
     Holt, Dennis A.; Keenan, Terence P.; Guo, Tao; Laborde, Edgardo; Yang, Wu
IN
     Ariad Gene Therapeutics, Inc., USA; Holt, Dennis A.; Keenan, Terence P.;
PA
     Guo, Tao; Laborde, Edgardo; Yang, Wu
     PCT Int. Appl., 98 pp.
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     1997:594714 CAPLUS
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ΤI
     Synthetic derivatives of rapamycin as multimerizing agents for chimeric
     proteins with immunophilin-derived domains
IN
     Holt, Dennis A.; Keenan, Terence P.; Guo, Tao; Laborde, Edgardo; Yang, Wu
     Ariad Gene Therapeutics, Inc., USA; Holt, Dennis A.; Keenan, Terence P.;
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     Guo, Tao; Laborde, Edgardo; Yang, Wu
     PCT Int. Appl., 116 pp.
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1997:594715 CAPLUS

AN

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TI
    Catalytic antibodies for activation of carbamate-containing prodrugs and
    their use in ADAPT (Antibody-Directed Abzyme Prodrug Therapy)
IN
    Blackburn, George Michael; Wentworth, Paul
PA
    Zeneca Limited, UK
    Eur. Pat. Appl., 141 pp.
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    1996:417799 CAPLUS
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    125:86501
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ΤI
    Preparation of linked piperidinecarboxylate moieties as immunophilin
    multimerizing agents
IN
    Holt, Dennis A.; Schreiber, Stuart; Keenan, Terence; Guo, Tao; Laborde,
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    PCT Int. Appl., 55 pp.
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    ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
L9
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    1995:996981 CAPLUS
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    124:176815
ΤI
    Preparation of vitamin B12 derivatives as receptor modulating agents for
    treating cancers
    Morgan, A. Charles; Wilbur, D. Scott; Pathare, Pradip M.
ΙN
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    USA
SO
    PCT Int. Appl., 101 pp.
    CODEN: PIXXD2
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L9
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    A new achiral reagent for the incorporation of multiple amino groups into
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TM, TT

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oligonucleotides
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     Behrens, Carsten; Petersen, Kenneth H.; Egholm, Michael; Nielsen, John;
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     Dep. Chem., Univ. Copenhagen, Copenhagen, DK-2100, Den.
     Bioorganic & Medicinal Chemistry Letters (1995), 5(16), 1785-90
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     Trifunctional conjugation reagents. Reagents that contain a biotin and a
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     Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.;
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     Department of Radiation Oncology, University of Washington, Seattle, WA,
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L12 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
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2001:923565 CAPLUS

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     Wilbur, D. Scott; Hamlin, Donald K.; Vessella, Robert L.; Stray, James E.;
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     Department of Radiation Oncology, University of Washington, Seattle, WA,
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     Bio Merieux, Fr.; Universite Joseph Fourier (Grenoble 1); Centre National
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     Indicator dyes, their production and their use in detecting biological
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IN
     Bourget, Cecile; Lhomme, Jean; Laayoun, Ali; Kotera, Mitsuharu; Trevisiol,
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     Bio Merieux, Fr.; Universite Joseph Fourier (Grenoble 1); Centre National
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     Trifunctional conjugation reagents. Reagents that contain a biotin
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     Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.;
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     Department of Radiation Oncology, University of Washington, Seattle, WA,
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    Biotin derivatives for an extracorporeal device
IN
     Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune
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    Mitra Medical Technology AB, Swed.; University of Washington
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     Aclara Biosciences, Inc., USA
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     Peptide and small molecule microarray for high throughput cell adhesion
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     Falsey, James R.; Renil, M.; Park, Steven; Li, Shijun; Lam, Kit S.
     UC Davis Cancer Center Division of Hematology/Oncology and Department of
CS
     Internal Medicine, University of California Davis, Sacramento, CA, 95817,
     Bioconjugate Chemistry (2001), 12(3), 346-353
SO
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     Surface Characterization of Mixed Self-Assembled Monolayers Designed for
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     Nelson, Kjell E.; Gamble, Lara; Jung, Linda S.; Boeckl, Maximiliane S.;
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     G.; Campbell, Charles T.; Stayton, Patrick S.
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Department of Bioengineering Department of Chemistry and Department of

Langmuir (2001), 17(9), 2807-2816

Chemical Engineering, University of Washington, Seattle, WA, 98195, USA

CS

SO

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AN
TΤ
     Synthesis and evaluation of protein biotinylation reagents that also
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ΑU
     Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Sandberg, Bengt E.
CS
     Radiation Oncology, University of Washington, Seattle, WA, 98103, USA
     Abstr. Pap. - Am. Chem. Soc. (2001), 221st, MEDI-031
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L13 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS
AN
     2000:145059 CAPLUS
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     Rapid quantitative analysis of proteins or protein function in complex
ΤI
     mixtures using affinity labeling reagents and mass spectrometry
     Aebersold, Rudolf Hans; Gelb, Michael H.; Gygi, Steven P.; Scott, C.
IN
     Ronald; Turecek, Frantisek; Gerber, Scott A.; Rist, Beate
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     University of Washington, USA
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TΙ
     Site-Specific Modification of a Single-Chain Antibody Using a Novel
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ΑU
     Zhao, Zhan G.; Im, Jin S.; Lam, Kit S.; Lake, Douglas F.
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Arizona Cancer Center, Tucson, AZ, 85724, USA

Bioconjugate Chemistry (1999), 10(3), 424-430

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TТ
     Biotin Reagents for Antibody Pretargeting. 2. Synthesis and in
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ΑU
     Wilbur, D. Scott; Pathare, Pradip M.; Hamlin, Donald K.; Weerawarna, S.
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     Department of Radiation Oncology, University of Washington, Seattle, WA,
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     Wilbur, Scott D.; Pathare, Pradip M.; Weerawarna, S. Ananda; Hamlin,
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ΤI
     Biotin reagents for antibody pretargeting. Synthesis,
     radioiodination and in vitro evaluation of water soluble, biotinidase
     resistant biotin derivatives
ΑU
     Wilbur, D. Scott; Hamlin, Donald K.; Pathare, Pradip M.; Weerawarna, S.
CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
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Bioconjugate Chemistry (1997), 8(4), 572-584
SO
     CODEN: BCCHES; ISSN: 1043-1802
PΒ
     American Chemical Society
DT
     Journal
LΑ
     English
L13
     ANSWER 14 OF 15 CAPLUS COPYRIGHT 2003 ACS
AN
     1997:155067 CAPLUS
DN
     126:207193
     Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin Ring Carboxylates and Evaluation of Their Binding to Transcobalamin. 2
ΤI
ΑU
     Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon;
     Quadros, Edward V.; McLoughlin, Patricia; Morgan, A. Charles
CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
     Bioconjugate Chemistry (1997), 8(2), 161-172
SO
     CODEN: BCCHES; ISSN: 1043-1802
PB
     American Chemical Society
DT
     Journal
     English
LΑ
L13 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2003 ACS
     1996:664622 CAPLUS
AN
DN
     126:3868
TΙ
     Antibody Fragments in Tumor Pretargeting. Evaluation of Biotinylated Fab'
     Colocalization with Recombinant Streptavidin and Avidin
     Wilbur, D. Scott; Hamlin, Donald K.; Vessella, Robert L.; Stray, James E.; Buhler, Kent R.; Stayton, Patrick S.; Klumb, Lisa A.; Pathare, Pradip M.;
AU
     Weerawarna, S. Ananda
CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
SO
     Bioconjugate Chemistry (1996), 7(6), 689-702
     CODEN: BCCHES; ISSN: 1043-1802
PB
     American Chemical Society
DT
     Journal
LΑ
     English
=> d his
     (FILE 'HOME' ENTERED AT 12:48:52 ON 16 JAN 2003)
     FILE 'REGISTRY' ENTERED AT 12:48:58 ON 16 JAN 2003
                 E AMINOISOPHTHALIC
L1
              66 S E1-E6
L2
               0 S FILE CAPLUS
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L3
             597 S L1
                 E BIOTIN
L4
           22854 S E3
L5
              15 S L3 AND L4
                 E LINKER
L6
           12580 S E3
L7
              17 S L3 AND L6
L8
              10 S L5 AND L7
               7 S L7 NOT L5
L9
L10
              71 S TRIDECANEDIAMINE
L11
            6520 S AVIDIN
L12
              3 S L10 AND L11
L13
              15 S L10 AND L4
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=> s 113 not 15 12 L13 NOT L5 => s 113 not 17 14 L13 NOT L7 => s 115 not 114 2 L15 NOT L14 L16 => d l16 1-2 all L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS AN 2002:523951 CAPLUS DN 137:228855 TITrifunctional conjugation reagents. Reagents that contain a biotin and a radiometal chelation moiety for application to extracorporeal affinity adsorption of radiolabeled antibodies ΑU Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.; Nilsson, Rune; Sandberg, Bengt E. B.; Brechbiel, Martin CS Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA SO Bioconjugate Chemistry (2002), 13(5), 1079-1092 CODEN: BCCHES; ISSN: 1043-1802 PB American Chemical Society DTJournal English LΑ CC 9-14 (Biochemical Methods) Section cross-reference(s): 8, 15, 63 AΒ A method of removing radiolabeled monoclonal antibodies (mAbs) from blood using a device external to the body, termed extracorporeal affinity-adsorption (EAA), is being evaluated as a means of decreasing irradn. of noncancerous tissues in therapy protocols. The EAA device uses an avidin column to capture biotinylated-radiolabeled mAbs from circulated blood. In this investigation, three trifunctional reagents have been developed to minimize the potential deleterious effect on antigen binding brought about by the combination of radiolabeling and biotinylation of mAbs required in the EAA approach. The studies focused on radiolabeling with 111In and 90Y, so the chelates CHX-A''-DTPA and DOTA, which form stable attachments to these radionuclides, were incorporated in the trifunctional reagents. The first trifunctional reagent prepd. did not incorporate a group to block the biotin cleaving enzyme biotinidase, but the two subsequent reagents coupled aspartic acid to the biotin carboxylate for that purpose. All three reagents used 4,7,10-trioxa-1,13-tridecanediamine as water-sol. spacers between an aminoisophthalate core and the biotin or chelation group. The mAb conjugates were radioiodinated to evaluate cell binding as a function of substitution. Radioiodination was used so that a direct comparison with unmodified mAb could be made. Evaluation of the no. of conjugates per antibody vs. cell binding immunoreactivities indicated that minimizing the no. of conjugates was best. Interestingly, a decrease of radioiodination yield as a function of the no. of isothiocyanate contg. conjugates per mAb was noted. The decreased yields were presumably due to the presence of thiourea functionality formed in the conjugation reaction.

Radiolabeling with 111In and 90Y was facile at room temp. for conjugates contg. the CHX-A'', but elevated temp. (e.g., 45.degree.) was required to obtain good yields with the DOTA chelate. Stability of 90Y labeled mAb in serum, and when challenged with 10 mM EDTA, was high. However, challenging the 90Y labeled mAb with 10 mM DTPA demonstrated high stability for the DOTA contg. conjugate, but low stability for the CHX-A'' contg. conjugate. Thus, the choice between these two chelating moieties might be made on requirements for facile and gentle labeling vs. very high in vivo

stability. Application of the trifunctional biotinylation reagents to the

```
new reagents may also be useful for other applications.
ST
     trifunctional conjugation reagent biotin radiometal chelation
ΙT
     Antibodies
     RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL
     (Biological study); PROC (Process)
        (monoclonal; trifunctional conjugation reagents. reagents that contain
        biotin and radiometal chelation moiety for application to
        extracorporeal affinity adsorption of radiolabeled antibodies)
IT
     Affinity
     Blood analysis
     Blood serum
     Chelation
        (trifunctional conjugation reagents. reagents that contain
        biotin and radiometal chelation moiety for application to
        extracorporeal affinity adsorption of radiolabeled antibodies)
IT
     Chelates
     Radionuclides, analysis
     RL: ARU (Analytical role, unclassified); ANST (Analytical study)
        (trifunctional conjugation reagents. reagents that contain
        biotin and radiometal chelation moiety for application to
        extracorporeal affinity adsorption of radiolabeled antibodies)
IT
     10098-91-6, Yttrium-90, analysis
                                        15750-15-9, Indium-111, analysis
     RL: ARU (Analytical role, unclassified); ANST (Analytical study)
        (trifunctional conjugation reagents. reagents that contain
        biotin and radiometal chelation moiety for application to
        extracorporeal affinity adsorption of radiolabeled antibodies)
IT
     99-31-0
               127985-74-4
                             137174-07-3
                                           178446-63-4
                                                          183896-00-6
     194920-62-2
                   295322-53-1
                                 459134-72-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (trifunctional conjugation reagents. reagents that contain
        biotin and radiometal chelation moiety for application to
        extracorporeal affinity adsorption of radiolabeled antibodies)
     380607-61-4P
ΙT
                    459134-70-4P
                                   459134-73-7P
                                                  459134-74-8P
                                                                  459134-75-9P
     459134-76-0P
                    459409-35-9P
                                   459409-37-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (trifunctional conjugation reagents. reagents that contain
        biotin and radiometal chelation moiety for application to
        extracorporeal affinity adsorption of radiolabeled antibodies)
TT
     459134-77-1P
                    459134-78-2P
                                   459409-36-0P
                                                 459409-38-2P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (trifunctional conjugation reagents. reagents that contain
        biotin and radiometal chelation moiety for application to
        extracorporeal affinity adsorption of radiolabeled antibodies)
              THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
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blood clearance of labeled antibodies in EAA is under investigation. The

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L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN
     2001:923565
                 CAPLUS
DN
     136:42919
     Biotin derivatives for an extracorporeal device
TΙ
IN
     Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune
     Mitra Medical Technology AB, Swed.; University of Washington
SO
     PCT Int. Appl., 45 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM A61K
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CC

63-7 (Pharmaceuticals)

Section cross-reference(s): 26 FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE \_\_\_\_\_\_ WO 2001095857 A2 20011220 PΙ WO 2001-SE1374 20010618 A3 20020328 WO 2001095857 W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 2002159994 A1 20021031 US 2001-881213 20010615 A5 20011224 AU 2001074761 AU 2001-74761 20010618 PRAI SE 2000-2287 A 20000616 US 2000-216625P P 20000707 WO 2001-SE1374 W 20010618 AB A method for the conditioning of an extracorporeal device is described, as well as a method for extracorporeal extn. of toxic material from mammalian body fluids in connection with diagnosis or treatment of a mammalian condition or disease. The methods comprise (i) a soln. contg. a reagent comprising biotin moieties, such as natural biotin or its derivs., and a toxin-binding moiety, (ii) linkers and a trifunctional crosslinking moiety, and (ii) an extracorporeal device comprising said reagent. For example, a dibiotin compd., 1-isothiocyanato-3,5-bis-(13'biotinamidyl-4',7',10'-trioxatridecanamidyl)-aminoisophthalate was prepd. and conjugated with a toxin-binding mol., i.e., monoclonal antibody 53-6A2. A dibiotin-toxin-binding conjugate was used for conditioning of an avidin-agarose column suitable for removal of toxins from blood. biotin deriv prepn reagent extracorporeal toxin extn; body fluid ST toxin extn extracorporeal biotin reagent ΤT Histocompatibility antigens RL: BSU (Biological study, unclassified); BIOL (Biological study) (HLA, antibodies against; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) IT Imaging (NMR; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids in diagnosis and therapy) IT Intercalation (agents; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) IT Antibodies RL: REM (Removal or disposal); PROC (Process) (anti-blood group; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) ΙT Blood-group substances RL: BSU (Biological study, unclassified); BIOL (Biological study) (antibodies against; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) ΙT Avidins

RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological

(biotin derivs.-binding coatings; prepn. of biotin

study); USES (Uses)

derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) IT Immunity (cells involved in, removal of; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) IT Avidins RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (conjugates, with agarose; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) IT Animal cell (diseased, removal of; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) IΤ Toxins RL: REM (Removal or disposal); PROC (Process) (endotoxins; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) ΙT Toxins RL: REM (Removal or disposal); PROC (Process) (enterotoxins; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) IT Circulation Extraction (extracorporeal; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) IT Chelating agents (for radionuclides; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) TΤ Immunoglobulins RL: REM (Removal or disposal); PROC (Process) (fragments; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) IT Antibodies RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (monoclonal, conjugates, with dibiotin compd.; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) ΙT Antibodies RL: REM (Removal or disposal); PROC (Process) (monoclonal; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) Amino group ΙT Blood Body fluid Carboxyl group Chemotherapy Cytotoxic agents Dyes Extraction columns Hydroxyl group (prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids)

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ΙT
     Chelates
     Cytokines
     Metals, processes
     Oligodeoxyribonucleotides
     Peptides, processes
     Radionuclides, processes
     Toxins
     Tumor necrosis factors
     RL: REM (Removal or disposal); PROC (Process)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
ΙT
     Diagnosis
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids in
        diagnosis and disease treatment)
IT
     Positron-emission tomography
     Scintigraphy
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids in
        diagnosis and therapy)
IT
     Transplant and Transplantation
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids prior to
        transplantation)
ΙT
     Bacteria (Eubacteria)
     Virus
        (toxins; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
IT
     Disease, animal
        (treatment; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids in diagnosis and disease treatment)
IT
     Reagents
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (tribiotinylated; prepn. of biotin derivs. for conditioning
        of extracorporeal device and extn. of toxic material from mammalian
        body fluids)
IT
     Neoplasm
        (uptake, monitoring of; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic material from
        mammalian body fluids)
     Antibodies
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (xenoantibodies, antibodies against; prepn. of biotin derivs.
        for conditioning of extracorporeal device and extn. of toxic material
        from mammalian body fluids)
IT
     9013-20-1, Streptavidin
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (biotin derivs.-binding coatings; prepn. of biotin
        derivs. for conditioning of extracorporeal device and extn. of toxic
        material from mammalian body fluids)
     9012-36-6D, Agarose, conjugates with avidin
IT
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
     58-85-5, Biotin
                      99-31-0, 5-Aminoisophthalic acid
                                                           4246-51-9,
                                          24424-99-5, Di-tert-butyl
     4,7,10,Trioxa-1,13-tridecanediamine
                  142685-25-4, 2,3,5,6-Tetrafluorophenyl trifluoroacetate
     dicarbonate
     380607-49-8
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RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
     173341-32-7P
                    178446-63-4P
                                   183896-00-6P
                                                  380607-50-1P
                                                                 380607-51-2P
     380607-56-7P
                    380607-60-3P
                                   380607-61-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
     380607-52-3P
                    380607-54-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
     USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
     194920-56-4P
                   194920-58-6P
                                  380607-48-7P
                                                 380607-52-3DP, conjugates
     with monoclonal antibodies
                                  380607-53-4P
                                                 380607-55-6P
                                                                380607-57-8P
     380607-58-9P
                    380607-59-0P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
ΙT
     533-48-2, Desthiobiotin
                               535-87-5, 3,5-Diaminobenzoic acid 554-95-0,
     1,3,5-Benzene tricarboxylic acid
                                       669-72-7, Nor-biotin
                           3376-83-8, Biotin sulfoxide
     1784-22-1, Homobiotin
     13395-35-2, Iminobiotin
                             14474-91-0, Oxybiotin
                                                       22342-46-7,
     Diaminobiotin
                     40720-05-6, Biotin sulfone
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
ΙT
     58-85-5D, Biotin, derivs.
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (radiolabeled; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from mammalian body
        fluids)
=> d l15 8-15 all
L15 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2003 ACS
ΑN
     2001:201927 CAPLUS
     Synthesis and evaluation of protein biotinylation reagents that also
TТ
     contain UV and/or fluorescence absorbing moieties
ΑU
     Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Sandberg, Bengt E.
CS
     Radiation Oncology, University of Washington, Seattle, WA, 98103, USA
    Abstr. Pap. - Am. Chem. Soc. (2001), 221st, MEDI-031
SO
     CODEN: ACSRAL; ISSN: 0065-7727
PΒ
    American Chemical Society
     Journal; Meeting Abstract
DT
LΑ
     English
AΒ
     Two new biotinylation reagents have been prepd. The reagents are
     trifunctional in that they contain a biotin moiety, a
     fluorescein or cyanocobalamin moiety, and an amine reactive functionality,
     Ph isothiocyanate. The biotin moiety is stabilized from
    biotinidase cleavage by coupling with an aspartate moiety, and the
    biotin-aspartate is sepd. from the phenylisothiocyanate moiety by
     a linker mol., 4,7,10-trioxa-1,13-tridecanediamine. The UV and
     fluorescent absorbing moieties are also linked to the phenylisothiocyanate
    via the a trioxatridecanediamine moiety. The new biotinylation reagents
    were prepd. primarily for use when the amt. of protein being biotinylated
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is limited. Quantification of the no. of biotin moieties per

protein mol. is difficult using the std. HABA dye method when small (i.e .mu.g quantities) of protein are used. A comparison of the quantification of nos. of **biotin** moieties/protein obtained via the HABA method and those obtained by direct measurement from absorption in UV and fluorescence will be provided.

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L15
    ANSWER 9 OF 14 CAPLUS COPYRIGHT 2003 ACS
     2000:145059 CAPLUS
AN
     132:191408
DN
TI
     Rapid quantitative analysis of proteins or protein function in complex
     mixtures using affinity labeling reagents and mass spectrometry
IN
     Aebersold, Rudolf Hans; Gelb, Michael H.; Gygi, Steven P.; Scott, C.
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PA
     University of Washington, USA
SO
     PCT Int. Appl., 116 pp.
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DT
     Patent
LΑ
    English
IC
     ICM C120001-00
     ICS G01N033-573; G01N033-53; G01N033-567; G01N024-00
     9-5 (Biochemical Methods)
     Section cross-reference(s): 6, 7, 26
FAN.CNT 1
     PATENT NO.
                     KIND DATE
                                          APPLICATION NO.
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    WO 2000011208
PΤ
                     A1
                           20000302
                                          WO 1999-US19415 19990825
        W: AU, JP
        RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
            PT, SE
     AU 9956913
                           20000314
                      A1
                                         AU 1999-56913
                                                          19990825
     EP 1105517
                     A1
                           20010613
                                          EP 1999-943915
                                                          19990825
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
     JP 2002523058
                      Т2
                           20020730
                                         JP 2000-566460
                                                          19990825
     JP 3345401
                     B2
                          20021118
    US 2002076739
                     A1 20020620
                                        US 2001-839884
                                                          20010420
PRAI US 1998-97788P P
                           19980825
    US 1998-99113P
                     P
                          19980903
    US 1999-383062
                     A3 19990825
    WO 1999-US19415 W
                           19990825
OS
    MARPAT 132:191408
    Anal. reagents and mass spectrometry-based methods using these reagents
    for the rapid, and quant. anal. of proteins or protein function in mixts.
    of proteins are disclosed. The methods employ affinity labeled protein
    reactive reagents having three portions: an affinity label (A) covalently
    linked to a protein reactive group (PRG) through a linker group (L). The
    linker may be differentially isotopically labeled, e.g., by substitution
    of one or more atoms in the linker with a stable isotope thereof. These
    reagents allow for the selective isolation of peptide fragments or the
    products of reaction with a given protein (e.g., products of enzymic
    reaction) from complex mixts. The isolated peptide fragments or reaction
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products are characteristic of the presence of a protein or the presence of a protein function in those mixts. Isolated peptides or reaction products are characterized by mass spectrometric (MS) techniques. The reagents also provide for differential isotopic labeling of the isolated peptides or reaction products which facilitates quant. detn. by mass spectrometry of the relative amt. of proteins in different samples. The methods of this invention can be used for qual. and quant. anal. of global protein expression profiles in cells and tissues, to screen for and identify proteins whose expression level in cells, tissue or biol. fluids is affected by a stimulus or by a change in condition or cell state of the cell, tissue or organism from which the sample originated. A conjugate of

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N-methylglycylbiotinamide acid and the Michael addn. product of
     4,7,10-trioxa-1,13-tridecanediamine and p-acrylamidophenyl-
     .beta.-D-galactopyranoside was prepd. for detecting .beta.-D-galactosidase
     deficiency and GM1-gangliosidosis.
    protein affinity labeling reagent mass spectrometry; isotope labeling
ST
     reagent protein mass spectrometry; function protein analysis; enzyme
     substrate affinity isotope label reagent; biotin conjugate
     reagent galactosidase GM1 gangliosidosis
IT
     Glycols, biological studies
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (1,2-, conjugates with labeled protein-reactive reagents; rapid quant.
        anal. of proteins or protein function in complex mixts. using affinity
        labeling reagents and mass spectrometry)
IT
    Gangliosidosis
        (GM1 gangliosidosis; rapid quant. anal. of proteins or protein function
        in complex mixts. using affinity labeling reagents and mass
        spectrometry)
IT
    Mucopolysaccharidosis
        (Sanfilippo's syndrome, type B or D; rapid quant. anal. of proteins or
        protein function in complex mixts. using affinity labeling reagents and
        mass spectrometry)
IT
     Enzymes, analysis
     RL: ANT (Analyte); BAC (Biological activity or effector, except adverse);
     BSU (Biological study, unclassified); THU (Therapeutic use); ANST
     (Analytical study); BIOL (Biological study); USES (Uses)
        (affinity labeling reagents contq. substrates for; rapid quant. anal.
        of proteins or protein function in complex mixts. using affinity
        labeling reagents and mass spectrometry)
ΙT
    Amino group
     Sulfhydryl group
        (affinity labeling reagents reactive with, of proteins; rapid quant.
        anal. of proteins or protein function in complex mixts. using affinity
        labeling reagents and mass spectrometry)
IT
     Carboxylic acids, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (affinity labeling reagents reactive with, of proteins; rapid quant.
        anal. of proteins or protein function in complex mixts. using affinity
        labeling reagents and mass spectrometry)
ΙT
     Peptides, analysis
     RL: ANT (Analyte); FMU (Formation, unclassified); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); FORM (Formation,
     nonpreparative); USES (Uses)
        (affinity-tagged, tagged proteins converted to; rapid quant. anal. of
        proteins or protein function in complex mixts. using affinity labeling
        reagents and mass spectrometry)
IT
     Protein sequence analysis
        (by tandem mass spectrometry; rapid quant. anal. of proteins or protein
        function in complex mixts. using affinity labeling reagents and mass
        spectrometry)
ΙT
    Haptens
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (conjugates, with labeled protein-reactive reagents; rapid quant. anal.
        of proteins or protein function in complex mixts. using affinity
        labeling reagents and mass spectrometry)
IT
    Tandem mass spectrometry
    Tandem mass spectrometry
        (electrospray-ionization; rapid quant. anal. of proteins or protein
        function in complex mixts. using affinity labeling reagents and mass
        spectrometry)
ΙT
    Congenital malformations
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Lysosomal storage disease (enzyme deficiency assocd. with; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Fibroblast

(enzyme reagent response to, of patients with and without .beta.-galactosidase deficiency; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Disease, animal

(enzyme-deficiency; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Avidins

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (immobilized, affinity column; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Disulfide group

(linker contg., in labeling reagents; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Mass spectrometry

Mass spectrometry

(liq. chromatog. combined with; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Liquid chromatography

Liquid chromatography

(mass spectrometry combined with; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Proteins, specific or class

RL: ANT (Analyte); ANST (Analytical study)

(membrane; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Stress, animal

(phys., proteins expressed in response to; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Saccharomyces cerevisiae

(protein expression in, with galactose or ethanol as carbon source; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Isotopes

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (protein-reactive affinity reagent labeled with; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Environment

Nutrition, animal

(proteins expressed in response to different conditions in; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Chemicals

(proteins expressed in response to different; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Organelle

(proteins of; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry)

IT Chromatography

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Functional groups
     Mass spectrometry
     Tandem mass spectrometry
     Test kits
        (rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
TΨ
     Proteins, general, analysis
     RL: AMX (Analytical matrix); ANT (Analyte); PRP (Properties); ANST
     (Analytical study)
        (rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
IT
     Ovalbumin
     RL: ANT (Analyte); RCT (Reactant); ANST (Analytical study); RACT (Reactant
     or reagent)
        (rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
IT
     Reagents
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
IT
     Cell
        (subcellular fractions of, proteins of; rapid quant. anal. of proteins
        or protein function in complex mixts. using affinity labeling reagents
        and mass spectrometry)
IT
     Electrospray ionization mass spectrometry
     Electrospray ionization mass spectrometry
        (tandem; rapid quant. anal. of proteins or protein function in complex
        mixts. using affinity labeling reagents and mass spectrometry)
ΙT
     Lactalbumins
     RL: ANT (Analyte); RCT (Reactant); ANST (Analytical study); RACT (Reactant
     or reagent)
        (.alpha.-; rapid quant. anal. of proteins or protein function in
        complex mixts. using affinity labeling reagents and mass spectrometry)
IT
     9031-11-2, .beta.-Galactosidase
                                       9032-94-4
                                                    37288-40-7
                                                                 37289-41-1,
                           60320-99-2, N-Acetylglucosamine-6-sulfatase
     Heparin sulfamidase
     RL: ANT (Analyte); BAC (Biological activity or effector, except adverse);
     BSU (Biological study, unclassified); THU (Therapeutic use); ANST
     (Analytical study); BIOL (Biological study); USES (Uses)
        (affinity labeling reagents contg. substrates for; rapid quant. anal.
        of proteins or protein function in complex mixts. using affinity
        labeling reagents and mass spectrometry)
ΙT
     1192-20-7, Homoserine lactone
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (affinity labeling reagents reactive with, of proteins; rapid quant.
        anal. of proteins or protein function in complex mixts. using affinity
        labeling reagents and mass spectrometry)
IT
     221565-10-2P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (as GM1 internal std.; rapid quant. anal. of proteins or protein
        function in complex mixts. using affinity labeling reagents and mass
        spectrometry)
IT
     259874-59-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (as deuterated analog; rapid quant. anal. of proteins or protein
        function in complex mixts. using affinity labeling reagents and mass
        spectrometry)
IT
     259874-28-7P
                    259874-29-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
     USES (Uses)
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(as enzyme substrate reagent; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) ΙT 221565-11-3P 259874-61-8P RL: SPN (Synthetic preparation); PREP (Preparation) (as internal std.; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) IT 259874-31-2 259874-32-3 RL: ARU (Analytical role, unclassified); ANST (Analytical study) (as labeled internal std.; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) 221565-07-7P ΙT RL: SPN (Synthetic preparation); PREP (Preparation) (as reagent for diagnosing Sanfilippo syndrome type B; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) TΤ 259874-55-0P RL: SPN (Synthetic preparation); PREP (Preparation) (as reagent for diagnosing Sanfilippo syndrome type D; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) ΙT 252730-69-1 252730-69-1D, deuterium-labeled RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses) (as reagent; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) IT 259874-30-1 RL: ANT (Analyte); FMU (Formation, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses) (enzyme reagent cleavage to; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) IT 58-85-5 107-13-1, 2-Propenenitrile, reactions 111-46-6, reactions 407-25-0, Trifluoroacetic anhydride 769-39-1, 2,3,5,6-Tetrafluorophenol 13515-93-0, N-Methylglycine methyl ester hydrochloride 182267-11-4 RL: RCT (Reactant); RACT (Reactant or reagent) (in prepn. of reagent for diagnosing GM1-gangliosidosis; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) 24997-19-1P 53807-26-4P, 2-Propenenitrile-2,3,3-d3 IT 22397-31-5P 112935-57-6P 142685-25-4P, 2,3,5,6-Tetrafluorophenyl trifluoroacetate 154024-76-7P 173341-32-7P 194920-70-2P 259874-33-4P 259874-35-6P 259874-36-7P 259874-38-9P 259874-39-0P 259874-40-3P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (in prepn. of reagent for diagnosing GM1-gangliosidosis; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) ΙT 221565-06-6P 259874-34-5P 259874-37-8P RL: SPN (Synthetic preparation); PREP (Preparation) (in prepn. of reagent for diagnosing GM1-gangliosidosis; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) IT 814-68-6, Acryloyl chloride RL: RCT (Reactant); RACT (Reactant or reagent) (in prepn. of reagent for diagnosing Sanfilippo syndrome type B; rapid quant. anal. of proteins or protein function in complex mixts. using affinity labeling reagents and mass spectrometry) ΙT 14419-59-1P 135253-87-1P 3386-87-6P 259874-41-4P 259874-42-5P

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259874-43-6P
                    259874-47-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (in prepn. of reagent for diagnosing Sanfilippo syndrome type B; rapid
        quant. anal. of proteins or protein function in complex mixts. using
        affinity labeling reagents and mass spectrometry)
TT
     259874-45-8P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (in prepn. of reagent for diagnosing Sanfilippo syndrome type B; rapid
        quant. anal. of proteins or protein function in complex mixts. using
        affinity labeling reagents and mass spectrometry)
IT
     259874-51-6P
                   259874-53-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (in prepn. of reagent for diagnosing Sanfilippo syndrome type D; rapid
        quant. anal. of proteins or protein function in complex mixts. using
        affinity labeling reagents and mass spectrometry)
     693-57-2
IT
               1670-26-4, Sphingosylphosphorylcholine
                                                         2238-90-6, Psychosine
     2997-01-5
                 4246-51-9
                             259874-25-4
                                           259874-26-5
                                                         259874-27-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (in reagent prepn.; rapid quant. anal. of proteins or protein function
        in complex mixts. using affinity labeling reagents and mass
        spectrometry)
IT
     183896-00-6P
                    259874-63-0P
                                   259874-66-3P
                                                  259874-74-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (in reagent prepn.; rapid quant. anal. of proteins or protein function
        in complex mixts. using affinity labeling reagents and mass
        spectrometry)
IT
     259874-68-5P
                    259874-70-9P
                                   259874~76-5P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (in reagent prepn.; rapid quant. anal. of proteins or protein function
        in complex mixts. using affinity labeling reagents and mass
        spectrometry)
ΙT
     59-23-4, Galactose, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BUU
     (Biological use, unclassified); BIOL (Biological study); PROC (Process);
     USES (Uses)
        (protein expression in Saccharomyces cerevisiae grown in ethanol or;
        rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
IT
     50-99-7, Glucose, miscellaneous
     RL: MSC (Miscellaneous)
        (protein expression in Saccharomyces cerevisiae grown in galactose or
        ethanol instead of; rapid quant. anal. of proteins or protein function
        in complex mixts. using affinity labeling reagents and mass
        spectrometry)
IT
     64-17-5, Ethanol; biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BUU
     (Biological use, unclassified); BIOL (Biological study); PROC (Process);
     USES (Uses)
        (protein expression in Saccharomyces cerevisiae grown in galactose or;
        rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
IT
     9001-50-7, Glyceraldehyde-3-phosphate dehydrogenase
     RL: ANT (Analyte); RCT (Reactant); ANST (Analytical study); RACT (Reactant
     or reagent)
        (rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
IT
     9013-20-1D, Streptavidin, agarose-immobilized
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (rapid quant. anal. of proteins or protein function in complex mixts.
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using affinity labeling reagents and mass spectrometry)
IT
     58-85-5D, Biotin, conjugates with labeled protein-reactive
                69-79-4D, Maltose, conjugates with labeled protein-reactive
     reagents
     reagents
                70-18-8D, Glutathione, conjugates with labeled protein-reactive
                71-00-1D, Histidine, oligo-, conjugates with labeled
     reagents
     protein-reactive reagents, biological studies
                                                    139-13-9D,
     Nitrilotriacetic acid, conjugates with labeled protein-reactive reagents
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
IT
     9001-92-7, Proteolytic enzyme
     RL: ARU (Analytical role, unclassified); CAT (Catalyst use); ANST
     (Analytical study); USES (Uses)
        (rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
     259874-57-2
TT
     RL: MSC (Miscellaneous)
        (rapid quant. anal. of proteins or protein function in complex mixts.
        using affinity labeling reagents and mass spectrometry)
ΙT
     9012-36-6, Agarose
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (streptavidin immobilized on; rapid quant. anal. of proteins or protein
        function in complex mixts. using affinity labeling reagents and mass
        spectrometry)
RE.CNT
        13
              THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
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(2) Berninger; US 5880270 A 1999 CAPLUS
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(7) Magnani; US 5965457 A 1999 CAPLUS
(8) Markert-Hahn; US 5514559 A 1996 CAPLUS
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(10) Shoseyov; US 5738984 A 1998 CAPLUS
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(13) Vreeke; US 5534132 A 1996 CAPLUS
L15 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2003 ACS
AΝ
     1999:255414 CAPLUS
DN
     131:70769
     Site-Specific Modification of a Single-Chain Antibody Using a Novel
ΤI
     Glyoxylyl-Based Labeling Reagent
ΑU
     Zhao, Zhan G.; Im, Jin S.; Lam, Kit S.; Lake, Douglas F.
     Arizona Cancer Center, Tucson, AZ, 85724, USA
CS
SO
     Bioconjugate Chemistry (1999), 10(3), 424-430
     CODEN: BCCHES; ISSN: 1043-1802
PΒ
     American Chemical Society
DT
     Journal
LA
     English
CC
     9-14 (Biochemical Methods)
     Section cross-reference(s): 2, 3, 15
AΒ
     A novel, highly specific protein modification approach is described. By
     using conventional mol. cloning techniques, a protein can be constructed
     and expressed such that the N-terminal residue is replaced by cysteine.
     Its 1,2-aminothiol structure reacts very specifically with a glyoxylyl
     group at pH 7 or below, forming a relatively stable thiazolidine bridge.
     Therefore, a glyoxylyl-based labeling agent (e.g., radioactive tags,
     fluorescent probes, biotin) can be used to specifically modify a
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protein at its N-terminus. To highlight this novel approach, a recombinant anti-insulin single chain antibody (scFv) was specifically biotinylated at its N-terminus even in the presence of other proteins in the total cell lysate. The glyoxylyl-biotinylated scFv retained binding activity similar to unmodified scFv. antibody labeling glyoxylyl biotin reagent; single chain antibody cloning glyoxylyl labeling Molecular cloning (of scFv, putting cysteine residue at N-terminus; site-specific modification of single-chain antibody using novel glyoxylyl-based labeling reagent) Escherichia coli (recombinant scFv expression in; site-specific modification of single-chain antibody using novel glyoxylyl-based labeling reagent) Antibodies RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent) (single chain; site-specific modification of single-chain antibody using novel glyoxylyl-based labeling reagent) 52-90-4, Cysteine, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent) (at N-terminus of scFv, mol. cloning in prepn. of and labeling reagent reactive with; site-specific modification of single-chain antibody using novel glyoxylyl-based labeling reagent) 58-85-5, **Biotin** 108-30-5, Succinic anhydride, reactions 4246-51-9, 4,7,10-Trioxa-1,13-tridecanediamine Fmoc-OSu RL: RCT (Reactant); RACT (Reactant or reagent) (in prepn. of glyoxylyl reagent; site-specific modification of single-chain antibody using novel glyoxylyl-based labeling reagent) 172089-14-4P 228851-40-9DP, resin-bound 228851-41-0DP, resin-bound RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (in prepn. of glyoxylyl reagent; site-specific modification of single-chain antibody using novel glyoxylyl-based labeling reagent) 228851-42-1DP, resin-bound RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and cleavage of, in prepn. of glyoxylyl reagent; site-specific modification of single-chain antibody using novel glyoxylyl-based labeling reagent) 228851-43-2P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and oxidn. of, in prepn. of glyoxylyl reagent; site-specific modification of single-chain antibody using novel glyoxylyl-based labeling reagent) 9004-10-8, Insulin, analysis RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process) (recombinant glyoxylyl-biotin-labeled scFv response to; site-specific modification of single-chain antibody using novel

(1) Alouni, S; Eur J Biochem 1995, V227, P328

glyoxylyl-based labeling reagent)

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RE.CNT RE THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(17) Sanger, F; Proc Natl Acad Sci U S A 1977, V74, P5463 CAPLUS
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(22) Zhang, L; Anal Biochem 1996, V233, P87 CAPLUS
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L15 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2003 ACS
AN
     1997:708440 CAPLUS
DN
     127:298612
ΤI
     Biotin Reagents for Antibody Pretargeting. 2. Synthesis and in
     Vitro Evaluation of Biotin Dimers and Trimers for Crosslinking
     of Streptavidin
ΑU
     Wilbur, D. Scott; Pathare, Pradip M.; Hamlin, Donald K.; Weerawarna, S.
CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
     Bioconjugate Chemistry (1997), 8(6), 819-832
SO
     CODEN: BCCHES; ISSN: 1043-1802
PB
     American Chemical Society
DT
     Journal
LΑ
     English
CC
     63-5 (Pharmaceuticals)
     Section cross-reference(s): 26
     Polymn. and/or crosslinking of recombinant streptavidin (r-SAv) with
AB
     biotin derivs. contg. two biotin moieties (
     biotin dimers) or three biotin moieties (biotin
     trimers) has been investigated as a model for reagents to be used to
     increase the amt. of radioactivity on cancer cells in tumor pretargeting
     protocols. In the investigation, six biotin dimers and three
     biotin trimers were synthesized. Most biotin derivs.
     synthesized had ether contg. linker mols. incorporated to improve their
     aq. soly. The synthesized biotin dimers contained linker
     moieties which provided distances (when fully extended) of 13-49 .ANG.
     between biotin carboxylate carbon atoms, and the biotin
     trimers contained linker moieties which provided distances of 31-53 .ANG.
     between any two biotin carboxylate atoms. All of the
     biotin derivs. were evaluated for their ability to polymerize
     r-SAv in soln. When the biotin derivs. were mixed with r-SAv,
     none of the biotin dimers caused polymn., but all of the
    biotin trimers resulted in complete polymn. Some of the
    biotin dimers did cross-link r-SAv (to form r-SAv dimers, trimers,
     etc.), but the percentage of crosslinking was low (.ltoreq.40%).
     length of the linker mol. was important in crosslinking of biotin
    dimers. While linkers which provided distances of 13 and 19 .ANG. between
    biotin carboxylate carbon atoms did not result in crosslinking, a
    linker which provided a 17 .ANG. distance resulted in a small
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(.ltoreq.10%) amt. of crosslinking. Also, crosslinking was increased in biotin dimers with linkers which provided distances between biotin carboxylate carbon atoms of .gtoreq.23 .ANG.. Crosslinking of streptavidin bound in polystyrene wells with biotin dimers and trimers was also examd. In those expts., an excess of each biotin deriv. was incubated at 37 .degree.C for 10-30 min in polystyrene wells contg. bound SAv. After the excess biotin deriv. was rinsed from the wells, an excess of r-[1251]SAv was incubated for another 10-30 min. The amt. of r-[1251] SAv bound after rinsing the excess from the wells was an indicator of the extent of crosslinking that occurred. The process of alternating addns. of reagents was repeated four times to demonstrate that bound radioactivity could be increased with each addn. of [1251] SAv. The results of crosslinking r-SAv in polystyrene wells paralleled results from crosslinking in soln. biotin oligomer prepn crosslinking streptavidin Crosslinking agents Immobilization, biochemical (prepn. and in vitro evaluation of biotin dimers and trimers for crosslinking of streptavidin) 9013-20-1, Streptavidin RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses) (prepn. and in vitro evaluation of biotin dimers and trimers for crosslinking of streptavidin) 58-85-5, **Biotin** 535-87-5, 3,5-Diaminobenzoic acid 3,6-Dioxa-1,8-octanediamine 4246-51-9, 4,7,10-Trioxa-1,13- **tridecanediamine** 4422-95-1, 1,3,5-Benzenetricarbonyl trichloride 13887-98-4, 3,6,9-Trioxaundecanedioic acid 142685-25-4 RL: RCT (Reactant); RACT (Reactant or reagent) (prepn. and in vitro evaluation of biotin dimers and trimers for crosslinking of streptavidin) 138529-46-1P 173341-32-7P 183896-00-6P 190250-18-1P 194920-45-1P 194920-46-2P 194920-54-2P 194920-55-3P 194920-56-4P 194920-58-6P 194920-64-4P 195152-91-1P 195152-92-2P 195152-94-4P 195152-96-6P 195152-98-8P 195152-99-9P 195153-00-5P 195370-62-8P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and in vitro evaluation of biotin dimers and trimers for crosslinking of streptavidin) L15 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2003 ACS 1997:542454 CAPLUS 127:220519 Preparation of biotin containing compounds with water soluble linker moieties for use as radionuclides and streptavidin crosslinking Wilbur, Scott D.; Pathare, Pradip M.; Weerawarna, S. Ananda; Hamlin, Donald K. Board of Regents of the University of Washington, USA PCT Int. Appl., 80 pp. CODEN: PIXXD2 Patent English ICM C07H015-00 ICS C12P013-18; C07D235-02; A01N043-52; A61K051-00 26-9 (Biomolecules and Their Synthetic Analogs) Section cross-reference(s): 1, 7, 8, 63 FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE WO 9729114 A1 19970814 WO 1997-US2560 19970207

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W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
             MR, NE, SN, TD, TG
     AU 9720524
                      A1
                            19970828
                                           AU 1997-20524
                                                            19970207
PRAI US 1996-11321P
                       Ρ
                            19960208
    WO 1997-US2560
                       W
                            19970207
GΙ
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$$H \longrightarrow H$$
 $H \longrightarrow H$ 
 $S \longrightarrow CO \longrightarrow Y \longrightarrow I$ 

$$H \sim N \sim H$$
 $H \sim N \sim H$ 
 $S \sim CO \sim NH \sim O \sim 2 \sim 11$ 

Water sol. biotin-contg. compds. and biotinylation reagents I {X = divalent water sol. linker such as NH(CH2)30(CH2)20(CH2)20(CH2)3NH, trivalent water sol. linker such as 1,3,5-C6H3[CONH(CH2)30(CH2)20(CH2)20(CH2)3NH]3; Y = reactive moiety such as 4-Bu3Sn-C6H4-CO; targeting, diagnostic, or therapeutic moiety such as 4-125I-C6H4-CO, biotin, or cyano-e-cobalamin} were prepd. for use as biotinylation reagents, biotinidase inhibitors (no data), and streptavidin cross linking agents. Thus, biotin dimer II was prepd. starting from biotin and 4,7,10-trioxa-1,13-tridecanediamine and was tested for streptavidin cross linking.

ST biotin compds prepn water soluble; biotinidase inhibitor water soluble biotin compd; streptavidin cross linking soluble biotin compd; biotinylation reagent soluble biotin compd; radionuclides water soluble biotin compd

IT Biotinylation

(prepn. of **biotin** contg. compds. with water sol. linker moieties for use as biotinylation reagents, radionuclides, biotinidase inhibitors, and streptavidin crosslinking agents)

IT Radionuclides, preparation

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of **biotin** contg. compds. with water sol. linker moieties for use as biotinylation reagents, radionuclides, biotinidase inhibitors, and streptavidin crosslinking agents)

IT 194920-54-2P 194920-55-3P 194920-56-4P 194920-58-6P 194920-60-0P 194920-61-1P

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study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (prepn. of biotin contg. compds. with water sol. linker
        moieties for use as biotinylation reagents, radionuclides, biotinidase
        inhibitors, and streptavidin crosslinking agents)
     9013-20-1, Streptavidin 9025-15-4, Biotinidase
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (prepn. of biotin contg. compds. with water sol. linker
        moieties for use as biotinylation reagents, radionuclides, biotinidase
        inhibitors, and streptavidin crosslinking agents)
     58-85-5, Biotin
ΙT
                       605-65-2, Dansyl chloride
                                                   929-59-9
     1711-02-0, 4-Iodobenzoyl chloride
                                         4246-51-9
                                                    4422-95-1,
     1,3,5-Benzenetricarbonyl trichloride
                                            4480-83-5, Diglycolic anhydride
     13515-93-0, N-Methylglycine methyl ester hydrochloride
                                                             26264-28-8
     55750-48-6, N-Methoxycarbonylmaleimide
                                             142685-25-4, 2,3,5,6-
     Tetrafluorophenyl trifluoroacetate
                                          172616-80-7
                                                       192720-54-0
     194920-72-4
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of biotin contg. compds. with water sol. linker
        moieties for use as biotinylation reagents, radionuclides, biotinidase
        inhibitors, and streptavidin crosslinking agents)
TΤ
     153086-78-3P
                   154024-76-7P
                                   173341-32-7P
                                                  175885-18-4P
                                                                 183896-00-6P
     188014-60-0P
                  192720-55-1P
                                   192720-56-2P
                                                  194920-44-0P
                                                                 194920-57-5P
     194920-62-2P
                   194920-63-3P
                                   194920-64-4P
                                                  194920-65-5P
                                                                 194920-66-6P
     194920-68-8P 194920-69-9P
                                   194920-70-2P
                                                  194920-71-3P
                                                                 194920-73-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of biotin contg. compds. with water sol. linker
        moieties for use as biotinylation reagents, radionuclides, biotinidase
        inhibitors, and streptavidin crosslinking agents)
ΙT
     183896-02-8P
                    194920-43-9P
                                   194920-59-7P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (prepn. of biotin contg. compds. with water sol. linker
        moieties for use as biotinylation reagents, radionuclides, biotinidase
        inhibitors, and streptavidin crosslinking agents)
IT
     189887-14-7P
                    194920-45-1P
                                  194920-46-2P
                                                  194920-47-3P
                                                                 194920-48-4P
     194920-50-8P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of biotin contg. compds. with water sol. linker
        moieties for use as biotinylation reagents, radionuclides, biotinidase
        inhibitors, and streptavidin crosslinking agents)
L15 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2003 ACS
AN
    1997:433652 CAPLUS
DN
    127:121587
TI
    Biotin reagents for antibody pretargeting. Synthesis,
     radioiodination and in vitro evaluation of water soluble, biotinidase
     resistant biotin derivatives
ΑU
    Wilbur, D. Scott; Hamlin, Donald K.; Pathare, Pradip M.; Weerawarna, S.
    Ananda
CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
     Bioconjugate Chemistry (1997), 8(4), 572-584
SO
    CODEN: BCCHES; ISSN: 1043-1802
PB
    American Chemical Society
DT
    Journal
LA
    English
CC
    26-8 (Biomolecules and Their Synthetic Analogs)
     Section cross-reference(s): 1, 15, 63
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *
AB
     An investigation was conducted to examine the stability of water
     solubilized, radioiodinated biotin derivs. toward biotinidase
     degrdn. in mouse and human serum as development of antibody pretargeting
     for cancer therapy. Eight new biotin derivs. were synthesized
     to conduct the study. The biotin derivs. synthesized contained (1) the biotin moiety, (2) a water solubilizing linker moiety,
     (3) p-iodobenzoate or p-tributylstannylbenzoate moieties, and (4) in some
     compds., N-Me or .alpha.-Me contg. moieties were added to block
     biotinidase activity. The linker moiety, 4,7,10-trioxa-1,13-
     tridecanediamine was included in the biotin derivs. to
     improve their water soly., and functioned as a 17 .ANG. spacer between the
     biotin and benzoyl moieties. Four of the new p-
     tributylstannylbenzoyl biotin derivs. I (R = H, Me; X = SnBu3),
     II (X = SnBu3), III (X = SnBu3) could be radioiodinated in the last
     synthetic step. The other four p-iodobenzoyl biotin derivs. I
     (R = H, Me; X = I), II (X = I), III (X = I) were used as HPLC ref. stds.
     Initial studies involved radioiodination of I (R = H; X = SnBu3) to yield
     [125I]-I (R = H; X = 125I). Radioiodinated I (R = H; X = I), did not
     contain a moiety for blocking biotinidase activity and was found to be
     rapidly degraded in both mouse and human serum at 37 .degree.C. Derivs.
     designed to be stable to biotinidase incorporated N-Me and .alpha.-Me
     moieties adjacent to the biotin carboxylate group. Linkers in
     the biotin derivs. were 4,7,10-trioxa-1,13-
     tridecanediamine, its N,N-di-Me analog or sarcosine
     (N-methylglycine). The radioiodinated N-Me contg. biotin
     derivs. I (R = Me; X = 125I) and II (X = 125I) were very stable to
     biotinidase degrdn. The radioiodinated .alpha.-Me contg. deriv., III (X =
     125I), has an intermediate stability with regards to biotinidase degrdn.
ST
     radioiodinated biotin analog prepn stability; water soluble
     biotin analog prepn stability; biotinidase resistant
     biotin analog prepn; sarcosine benzoyltrioxadiamine biotin
     analog prepn
TΤ
     Antibodies
     RL: PNU (Preparation, unclassified); PREP (Preparation)
        (conjugates; prepn. of stable biotin analogs for antibody
        targeting)
ΙT
     Antitumor agents
        (prepn. of stable biotin analogs for antibody targeting)
ΙT
     192720-95-9P
                   192720-97-1P 192720-99-3P 192721-01-0P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); BIOL (Biological
     study); PREP (Preparation)
        (synthesis, radioiodination and in vitro evaluation of water sol.,
        biotinidase resistant biotin derivs.)
IT
     9025-15-4, Biotinidase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (synthesis, radioiodination and in vitro evaluation of water sol.,
        biotinidase resistant biotin derivs.)
IT
     541-48-0, 3-Aminobutyric acid 619-58-9, 4-Iodobenzoic acid
                                                                     769-39-1,
     2,3,5,6-Tetrafluorophenol
                                 4246-51-9
                                             13515-93-0, N-Methylglycine methyl
     ester hydrochloride
                           192720-58-4
                                         192720-61-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (synthesis, radioiodination and in vitro evaluation of water sol.,
        biotinidase resistant biotin derivs.)
     95708-93-3P 110345-46-5P 192720-53-9P
ΙT
                                                  192720-54-0P
                                                                 192720-55-1P
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192720-56-2P
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              192720-86-8P
                             192720-93-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
   (synthesis, radioiodination and in vitro evaluation of water sol.,
  biotinidase resistant biotin derivs.)
192720-66-4P
             192720-70-0P 192720-88-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
   (synthesis, radioiodination and in vitro evaluation of water sol.,
  biotinidase resistant biotin derivs.)
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- L15 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2003 ACS
- AN 1996:664622 CAPLUS
- DN 126:3868

ΙT

- TI Antibody Fragments in Tumor Pretargeting. Evaluation of Biotinylated Fab' Colocalization with Recombinant Streptavidin and Avidin
- AU Wilbur, D. Scott; Hamlin, Donald K.; Vessella, Robert L.; Stray, James E.; Buhler, Kent R.; Stayton, Patrick S.; Klumb, Lisa A.; Pathare, Pradip M.; Weerawarna, S. Ananda
- CS Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
- SO Bioconjugate Chemistry (1996), 7(6), 689-702 CODEN: BCCHES; ISSN: 1043-1802
- PB American Chemical Society
- DT Journal
- LA English

AΒ

- CC 8-9 (Radiation Biochemistry)
  Section cross-reference(s): 14
  - An evaluation of the use of a biotinylated monoclonal antibody Fab' fragment in tumor pretargeting was conducted. As a model system, tumor colocalization of avidin or recombinant streptavidin (r-streptavidin) and the biotinylated Fab' fragment (Fab'-S-biotin) of A6H, an antirenal cell carcinoma antibody, was evaluated in athymic mice bearing human renal cell carcinoma xenografts. A new water sol. sulfhydryl reactive biotinylation reagent, N-(13-N-maleimido-4,7,10trioxatridecanyl)biotinamide, was synthesized and used for biotinylation of Fab'. A biodistribution of ChT-labeled A6H Fab'-S-biotin was conducted. Data from that distribution indicated that the Fab'-Sbiotin localized well (i.e. 28% ID/q at 24 h) to human tumor xenografts in athymic mice. Subsequently, a biodistribution study involving pretargeting radioiodinated A6H Fab'-S-biotin to tumor xenografts, followed by administration of r-streptavidin at 4 or 20 h, was conducted. Specific colocalization of r-streptavidin to tumors contq. the A6H Fab'-S-biotin was evident from the data obtained. In a similar biodistribution study, specific colocalization of avidin to tumors pretargeted with A6H Fab'-S-biotin was also obsd. The avidin used in the study was radioiodinated with the N-hydroxysuccinimidyl ester of p-[125I]iodobenzoate ([125I]PIB-NHS). Very low concns. (e.g.  $\bar{0}.35\%$  ID/g) of avidin colocalized at the tumor. To further show that specific colocalization within the tumor xenografts had occurred with biotinylated A6H Fab', radioiodinated avidin and r-streptavidin were co-injected into athymic mice bearing tumor xenografts to obtain their distributions without having biotinylated Fab' present. At 20 h postinjection, only small differences in the blood and tumor concns. of either protein were obsd., indicating that the specific tumor colocalization seen in the previous two biodistributions must have been due to the presence of Fab'-S-biotin. Calcns. were conducted to est. how much r-streptavidin (as a molar ratio) was colocalized. From the data obtained it was estd. that 36-61% of the tumor-localized Fab'-S-biotin mols. were bound with r-streptavidin and 4-23% bound with avidin, under the conditions studied.

```
ST
     tumor pretargeting biotinylated monoclonal antibody
IT
     Antibodies
     RL: BPR (Biological process); BSU (Biological study, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (monoclonal, Fab', biotinylated; renal cell carcinoma pretargeting
        using biotinylated Fab' monoclonal antibody with recombinant
        streptavidin and avidin)
ΤТ
     Avidins
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (renal cell carcinoma pretargeting using biotinylated Fab' monoclonal
        antibody with recombinant streptavidin and avidin)
ΙT
     Kidney, neoplasm
        (renal cell carcinoma; renal cell carcinoma pretargeting using
        biotinylated Fab' monoclonal antibody with recombinant streptavidin and
        avidin)
IT
     173341-32-7P
                    183896-00-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (intermediate; renal cell carcinoma pretargeting using biotinylated
        Fab' monoclonal antibody with recombinant streptavidin and avidin)
     4246-51-9, 4,7,10-Trioxa-1,13-tridecanediamine 55750-48-6,
ΙT
     N-Methoxycarbonylmaleimide
                                 142685-25-4
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reactant; renal cell carcinoma pretargeting using biotinylated Fab'
        monoclonal antibody with recombinant streptavidin and avidin)
IT
     9013-20-1, Streptavidin
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (renal cell carcinoma pretargeting using biotinylated Fab' monoclonal
        antibody with recombinant streptavidin and avidin)
ΙT
     58-85-5, Biotin
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (renal cell carcinoma pretargeting using biotinylated Fab' monoclonal
        antibody with recombinant streptavidin and avidin)
ΙT
     183896-02-8P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (renal cell carcinoma pretargeting using biotinylated Fab' monoclonal
        antibody with recombinant streptavidin and avidin)
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     FILE 'REGISTRY' ENTERED AT 12:48:58 ON 16 JAN 2003
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L1
             66 S E1-E6
L2
              0 S FILE CAPLUS
     FILE 'CAPLUS' ENTERED AT 12:51:32 ON 16 JAN 2003
L3
           597 S L1
                E BIOTIN
L4
          22854 S E3
L5
             15 S L3 AND L4
                E LINKER
          12580 S E3
L6
L7
            17 S L3 AND L6
L8
            10 S L5 AND L7
L9
             7 S L7 NOT L5
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L10
             71 S TRIDECANEDIAMINE
L11
           6520 S AVIDIN
L12
              3 S L10 AND L11
L13
             15 S L10 AND L4
             12 S L13 NOT L5
L14
             14 S L13 NOT L7
L15
              2 S L15 NOT L14
L16
=> e extracorporeal
                   EXTRACORPORCALLY/BI
             1
E2
             2
                   EXTRACORPOREA/BI
E3
          5268 --> EXTRACORPOREAL/BI
E4
           133
                   EXTRACORPOREALLY/BI
E5
             1
                   EXTRACORPOREALS/BI
E6
             1
                   EXTRACORPORED/BI
E7
             1
                   EXTRACORPOREL/BI
F.8
             1
                   EXTRACORPOREOL/BI
E9
            1
                   EXTRACORPREAL/BI
E10
            25
                   EXTRACORPUSCULAR/BI
E11
            26
                   EXTRACORTICAL/BI
E12
            1
                   EXTRACOTYLEDONARY/BI
=> s e3-e11
          5268 EXTRACORPOREAL/BI
           133 EXTRACORPOREALLY/BI
             1 EXTRACORPOREALS/BI
             1 EXTRACORPORED/BI
             1 EXTRACORPOREL/BI
             1 EXTRACORPOREOL/BI
             1 EXTRACORPREAL/BI
            25 EXTRACORPUSCULAR/BI
            26 EXTRACORTICAL/BI
L17
          5404 (EXTRACORPOREAL/BI OR EXTRACORPOREALLY/BI OR EXTRACORPOREALS/BI
               OR EXTRACORPORED/BI OR EXTRACORPOREL/BI OR EXTRACORPOREOL/BI OR
               EXTRACORPREAL/BI OR EXTRACORPUSCULAR/BI OR EXTRACORTICAL/BI)
=> s 117 and 13
             4 L17 AND L3
=> d 118 1-4 all
L18 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
ΑN
     2002:523951 CAPLUS
DN
     137:228855
TΙ
     Trifunctional conjugation reagents. Reagents that contain a biotin and a
     radiometal chelation moiety for application to extracorporeal
     affinity adsorption of radiolabeled antibodies
ΑU
     Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.;
     Nilsson, Rune; Sandberg, Bengt E. B.; Brechbiel, Martin
     Department of Radiation Oncology, University of Washington, Seattle, WA,
CS
     98195, USA
SO
     Bioconjugate Chemistry (2002), 13(5), 1079-1092
     CODEN: BCCHES; ISSN: 1043-1802
PB
     American Chemical Society
DT
     Journal
LΑ
     English
CC
     9-14 (Biochemical Methods)
     Section cross-reference(s): 8, 15, 63
AΒ
     A method of removing radiolabeled monoclonal antibodies (mAbs) from blood
     using a device external to the body, termed extracorporeal
     affinity-adsorption (EAA), is being evaluated as a means of decreasing
     irradn. of noncancerous tissues in therapy protocols. The EAA device uses
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an avidin column to capture biotinylated-radiolabeled mAbs from circulated blood. In this investigation, three trifunctional reagents have been developed to minimize the potential deleterious effect on antigen binding brought about by the combination of radiolabeling and biotinylation of mAbs required in the EAA approach. The studies focused on radiolabeling with 111In and 90Y, so the chelates CHX-A''-DTPA and DOTA, which form stable attachments to these radionuclides, were incorporated in the trifunctional reagents. The first trifunctional reagent prepd. did not incorporate a group to block the biotin cleaving enzyme biotinidase, but the two subsequent reagents coupled aspartic acid to the biotin carboxylate for that purpose. All three reagents used 4,7,10-trioxa-1,13-tridecanediamine as water-sol. spacers between an aminoisophthalate core and the biotin or chelation group. The mAb conjugates were radioiodinated to evaluate cell binding as a function of substitution. Radioiodination was used so that a direct comparison with unmodified mAb could be made. Evaluation of the no. of conjugates per antibody vs. cell binding immunoreactivities indicated that minimizing the no. of conjugates was best. Interestingly, a decrease of radioiodination yield as a function of the no. of isothiocyanate contg. conjugates per mAb was noted. The decreased yields were presumably due to the presence of thiourea functionality formed in the conjugation reaction. Radiolabeling with 111In and 90Y was facile at room temp. for conjugates contg. the CHX-A'', but elevated temp. (e.g., 45.degree.) was required to obtain good yields with the DOTA chelate. Stability of 90Y labeled mAb in serum, and when challenged with 10 mM EDTA, was high. However, challenging the 90Y labeled mAb with 10 mM DTPA demonstrated high stability for the DOTA contg. conjugate, but low stability for the CHX-A'' contg. conjugate. Thus, the choice between these two chelating moieties might be made on requirements for facile and gentle labeling vs. very high in vivo stability. Application of the trifunctional biotinylation reagents to the blood clearance of labeled antibodies in EAA is under investigation. The new reagents may also be useful for other applications.

ST trifunctional conjugation reagent biotin radiometal chelation IT

Antibodies

RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)

(monoclonal; trifunctional conjugation reagents. reagents that contain biotin and radiometal chelation moiety for application to

extracorporeal affinity adsorption of radiolabeled antibodies)

Affinity IT

Blood analysis

Blood serum

Chelation

(trifunctional conjugation reagents. reagents that contain biotin and radiometal chelation moiety for application to extracorporeal affinity adsorption of radiolabeled antibodies)

IT Chelates

Radionuclides, analysis

RL: ARU (Analytical role, unclassified); ANST (Analytical study) (trifunctional conjugation reagents. reagents that contain biotin and radiometal chelation moiety for application to extracorporeal affinity adsorption of radiolabeled antibodies)

10098-91-6, Yttrium-90, analysis IT15750-15-9, Indium-111, analysis RL: ARU (Analytical role, unclassified); ANST (Analytical study) (trifunctional conjugation reagents. reagents that contain biotin and radiometal chelation moiety for application to extracorporeal affinity adsorption of radiolabeled antibodies)

IT 127985-74-4 99-31-0 137174-07-3 178446-63-4 183896-00-6 194920-62-2 295322-53-1 459134-72-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(trifunctional conjugation reagents. reagents that contain biotin and radiometal chelation moiety for application to extracorporeal

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affinity adsorption of radiolabeled antibodies)
IT
     380607-61-4P
                     459134-70-4P
                                    459134-73-7P
                                                    459134-74-8P
                                                                    459134-75-9P
     459134-76-0P
                     459409-35-9P
                                    459409-37-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (trifunctional conjugation reagents. reagents that contain biotin and
        radiometal chelation moiety for application to extracorporeal
        affinity adsorption of radiolabeled antibodies)
IT
     459134-77-1P
                   459134-78-2P
                                    459409-36-0P
                                                   459409-38-2P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (trifunctional conjugation reagents. reagents that contain biotin and
        radiometal chelation moiety for application to extracorporeal
        affinity adsorption of radiolabeled antibodies)
RE.CNT
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L18 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
     2001:923565 CAPLUS
ΑN
DN
     136:42919
TΙ
     Biotin derivatives for an extracorporeal device
IN
     Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune
     Mitra Medical Technology AB, Swed.; University of Washington
SO
     PCT Int. Appl., 45 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM A61K
CC
     63-7 (Pharmaceuticals)
     Section cross-reference(s): 26
FAN.CNT 1
     PATENT NO.
                      KIND DATE
                                            APPLICATION NO.
                                                              DATE
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                     A2
     WO 2001095857
                             20011220
                                            WO 2001-SE1374
                                                              20010618
     WO 2001095857
                      A3
                            20020328
            AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,
             FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
             MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ,
             TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 2002159994
                       A1
                           20021031
                                           US 2001-881213
                                                              20010615
     AU 2001074761
                       A5
                             20011224
                                            AU 2001-74761
                                                              20010618
PRAI SE 2000-2287
                             20000616
                       Α
     US 2000-216625P
                       Р
                             20000707
     WO 2001-SE1374
                       W
                             20010618
AΒ
    A method for the conditioning of an extracorporeal device is
     described, as well as a method for extracorporeal extn. of toxic
     material from mammalian body fluids in connection with diagnosis or
     treatment of a mammalian condition or disease. The methods comprise (i) a
     soln. contg. a reagent comprising biotin moieties, such as natural biotin
     or its derivs., and a toxin-binding moiety, (ii) linkers and a
     trifunctional crosslinking moiety, and (ii) an extracorporeal
     device comprising said reagent. For example, a dibiotin compd.,
     1-isothiocyanato-3,5-bis-(13'-biotinamidyl-4',7',10'-trioxatridecanamidyl)-
     aminoisophthalate was prepd. and conjugated with a toxin-binding mol.,
     i.e., monoclonal antibody 53-6A2. A dibiotin-toxin-binding conjugate was
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used for conditioning of an avidin-agarose column suitable for removal of
     toxins from blood.
ST
     biotin deriv prepn reagent extracorporeal toxin extn; body fluid
     toxin extn extracorporeal biotin reagent
     Histocompatibility antigens
TΤ
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (HLA, antibodies against; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
ΙT
     Imaging
        (NMR; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids in diagnosis and therapy)
ΙT
     Intercalation
        (agents; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Antibodies
     RL: REM (Removal or disposal); PROC (Process)
        (anti-blood group; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
TΤ
     Blood-group substances
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (antibodies against; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Avidins
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (biotin derivs.-binding coatings; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic
        material from mammalian body fluids)
IT
     Immunity
        (cells involved in, removal of; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic
        material from mammalian body fluids)
ΤТ
     Avidins
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (conjugates, with agarose; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Animal cell
        (diseased, removal of; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Toxins
     RL: REM (Removal or disposal); PROC (Process)
        (endotoxins; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Toxins
     RL: REM (Removal or disposal); PROC (Process)
        (enterotoxins; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
    Circulation
     Extraction
        (extracorporeal; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
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mammalian body fluids)

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IT
     Chelating agents
        (for radionuclides; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Immunoglobulins
     RL: REM (Removal or disposal); PROC (Process)
        (fragments; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Antibodies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (monoclonal, conjugates, with dibiotin compd.; prepn. of biotin derivs.
        for conditioning of extracorporeal device and extn. of toxic
        material from mammalian body fluids)
IT
     Antibodies
     RL: REM (Removal or disposal); PROC (Process)
        (monoclonal; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Amino group
     Blood
     Body fluid
     Carboxyl group
     Chemotherapy
     Cytotoxic agents
     Dyes
     Extraction columns
     Hydroxyl group
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
ΙT
     Chelates
     Cytokines
     Metals, processes
     Oligodeoxyribonucleotides
     Peptides, processes
     Radionuclides, processes
     Toxins
     Tumor necrosis factors
     RL: REM (Removal or disposal); PROC (Process)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
ΙT
     Diagnosis
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids in
        diagnosis and disease treatment)
     Positron-emission tomography
ΙT
     Scintigraphy
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids in
        diagnosis and therapy)
IT
     Transplant and Transplantation
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids prior to
        transplantation)
ΙT
     Bacteria (Eubacteria)
     Virus
        (toxins; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
     Disease, animal
        (treatment; prepn. of biotin derivs. for conditioning of
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extracorporeal device and extn. of toxic material from
        mammalian body fluids in diagnosis and disease treatment)
IT
     Reagents
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (tribiotinylated; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
       mammalian body fluids)
IT
     Neoplasm
        (uptake, monitoring of; prepn. of biotin derivs. for conditioning of
        extracorporeal device and extn. of toxic material from
        mammalian body fluids)
IT
    Antibodies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (xenoantibodies, antibodies against; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic
        material from mammalian body fluids)
     9013-20-1, Streptavidin
ΤТ
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (biotin derivs.-binding coatings; prepn. of biotin derivs. for
        conditioning of extracorporeal device and extn. of toxic
        material from mammalian body fluids)
ΤT
     9012-36-6D, Agarose, conjugates with avidin
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
     58-85-5, Biotin 99-31-0, 5-Aminoisophthalic acid
                                                       4246-51-9.
                                           24424-99-5, Di-tert-butyl
     4,7,10,Trioxa-1,13-tridecanediamine
                   142685-25-4, 2,3,5,6-Tetrafluorophenyl trifluoroacetate
     dicarbonate
     380607-49-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
     173341-32-7P
IT
                   178446-63-4P
                                   183896-00-6P
                                                  380607-50-1P
                                                                 380607-51-2P
     380607-56-7P
                    380607-60-3P
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     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
                    380607-54-5P
     380607-52-3P
     RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
    USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
IT
     194920-56-4P
                   194920-58-6P
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                                                 380607-52-3DP, conjugates
                                  380607-53-4P
                                                 380607-55-6P
                                                                380607-57-8P
    with monoclonal antibodies
     380607-58-9P
                   380607-59-0P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
        device and extn. of toxic material from mammalian body fluids)
ΙT
    533-48-2, Desthiobiotin 535-87-5, 3,5-Diaminobenzoic acid
                                                                   554-95-0,
     1,3,5-Benzene tricarboxylic acid 669-72-7, Nor-biotin
                                                               1784-22-1,
    Homobiotin
                3376-83-8, Biotin sulfoxide 13395-35-2, Iminobiotin
    14474-91-0, Oxybiotin 22342-46-7, Diaminobiotin 40720-05-6, Biotin
    sulfone
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal
       device and extn. of toxic material from mammalian body fluids)
IT
    58-85-5D, Biotin, derivs.
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (radiolabeled; prepn. of biotin derivs. for conditioning of extracorporeal device and extn. of toxic material from mammalian body fluids) ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS 2000:35037 CAPLUS 132:90367 Trifunctional reagent for conjugation to a biomolecule for use in diagnosis and therapy Wilbur, D. Scott; Sandberg, Bengt E. B. Dept. of Radiation Oncology, University of Washington, USA; Mitra Medical Technology AB PCT Int. Appl., 48 pp. CODEN: PIXXD2 Patent English ICM G01N033-543 ICS A61K039-00; A61K047-48; A61K051-00; A61K049-00 9-15 (Biochemical Methods) Section cross-reference(s): 1, 8, 15, 63 FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. -----\_\_\_\_\_ WO 2000002051 A1 20000113 WO 1999-SE1241 19990707 W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG WO 2000002050 A1 20000113 WO 1998-SE1345 19980707 AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG CA 2336739 20000113 CA 1999-2336739 AA 19990707 AU 9950767 Α1 20000124 AU 1999-50767 19990707 EP 1095274 Α1 20010502 EP 1999-935251 19990707 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO JP 2000-558395 JP 2002519440 Т2 20020702 19990707 US 2001023288 Α1 20010920 US 2000-750280 20001229 NO 2001000021 Α 20010307 NO 2001-21 20010103 PRAI WO 1998-SE1345 A 19980707 WO 1999-SE1241 W 19990707 A reagent for conjugation to a biomol. for diagnosis and treatment of human and animal conditions and diseases is described, wherein the reagent is a single mol. with at least three functional parts and a) wherein a trifunctional crosslinking moiety is coupled to b) an affinity ligand via a linker 1, said affinity ligand being capable of binding with another mol. having affinity for said ligand; to c) an effector agent, optionally via a linker 2, said effector agent exerting its effects on cells, tissues

and/or humorous mols. in vivo or ex vivo; and to d) a biomol. reactive

AN

DN ΤI

IN PA

SO

DT

LA IC

PΙ

AB

moiety, optionally via a linker 3, said moiety being capable of forming a bond between the reagent and the biomol. The affinity ligand is esp. biotin or a biotin deriv. The effector agent is a toxin, an enzyme capable of converting a prodrug to an active drug, an immunosuppressant, an immunostimulant, or a radionuclide-binding agent, with or without the radionuclide.

ST trifunctional reagent biomol conjugation diagnosis therapy; biotin trifunctional reagent biomol conjugate diagnosis therapy; toxin trifunctional reagent biomol conjugate therapy; prodrug converting enzyme trifunctional reagent conjugate; immunomodulator trifunctional reagent conjugate; radiotherapy trifunctional reagent conjugate; imaging agent trifunctional reagent conjugate

IT Imaging agents

(NMR contrast, trifunctional reagent contg., as effector agent; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Imaging agents

(acoustic imaging contrast agents, trifunctional reagent contg., as effector agent; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Proteins, specific or class

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(affinity ligand-binding, for removal of nontargeted biomol. conjugate from blood circulation; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Ligands

RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

(affinity, trifunctional reagent contg.; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Functional groups

(ammonio group, linkers contg.; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Chromophores

Fluorescent substances

(as effector agent in trifunctional reagent; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Separators

(blood plasma, in kit for removal of nontargeted biomol. conjugate from blood circulation; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Amines, biological studies

RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)

(cyclic, radionuclide-binding, as effector agent in trifunctional reagent; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Lung, disease

(embolism; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Carboxylic acids, properties

RL: PRP (Properties)

(esters, linkers contg.; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

IT Adsorption apparatus

(extracorporeal, in kit for removal of nontargeted biomol. conjugate from blood circulation; trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

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IT
     Circulation
        (extracorporeal, nontargeted biomol. conjugate removal from;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Affinity chromatographic stationary phases
        (for removal of nontargeted biomol. conjugate from blood circulation;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Imaging
        (gamma-ray; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
IT
     Vinyl compounds, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (halo, halogen radionuclide-contg., as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
TΤ
     Arvl halides
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (halogen radionuclide-contg., as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Avidins
     Receptors
     RL: BUU (Biological use, unclassified); DEV (Device component use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (immobilized, extracorporeal adsorption device contg., in kit
        for removal of nontargeted biomol. conjugate from blood circulation;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Heart, disease
        (infarction; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
TΤ
     Ethers, properties
     Sulfonates
     Thioethers
     RL: PRP (Properties)
        (linkers contg.; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     Circulation
        (nontargeted biomol. conjugate removal from; trifunctional reagent for
        conjugation to a biomol. for use in diagnosis and therapy)
IT
     Radiosensitizers, biological
        (pharmaceutical, trifunctional reagent contg., as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
    Materials
        (photoactive chems., as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Enzymes, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (prodrug-metabolizing, trifunctional reagent contg., as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
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and therapy)
ΙT
     Drug delivery systems
        (prodrugs, trifunctional reagent contg. enzymes metabolizing;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Brain, disease
        (stroke; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Radiotherapy
        (targeted; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
ΙT
     Disease, animal
        (treatment of; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     Avidins
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (trifunctional reagent contq. affinity ligand binding to; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
ΙT
     Body fluid
        (trifunctional reagent contg. effector agent acting on mols. in;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Animal tissue
     Cell
        (trifunctional reagent contg. effector agent acting on; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
IT
     Radionuclides, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (trifunctional reagent contg. moieties binding to, as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Immunostimulants
     Immunosuppressants
        (trifunctional reagent contg., as effector agent; trifunctional reagent
        for conjugation to a biomol. for use in diagnosis and therapy)
     Enzymes, biological studies
TΤ
     Hormones, animal, biological studies
     Toxins
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (trifunctional reagent contg., as effector agent; trifunctional reagent
        for conjugation to a biomol. for use in diagnosis and therapy)
IΤ
     Animal
     Atherosclerosis
     Biochemical molecules
     Diagnosis
     Drug targeting
     Mammal (Mammalia)
     Neoplasm
     Photodynamic therapy
     Photoimaging
     Positron-emission tomography
     Therapy
     Vertebrate (Vertebrata)
        (trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
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ΙT
     Reagents
     RL: ARG (Analytical reagent use); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); RACT (Reactant or
     reagent); USES, (Uses)
        (trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Crosslinking agents
        (trifunctional; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IΤ
     Thrombosis
        (venous, deep; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
ΙT
     Imaging agents
        (x-ray, contrast, trifunctional reagent contg., as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     9025-15-4, Biotinidase
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (biotin-contg. reagent with stability against cleavage with;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     7439-92-1D, Lead, radionuclides, biological studies
                                                           7439-94-3D.
     Lutetium, radionuclides, biological studies
                                                   7440-19-9D, Samarium,
     radionuclides, biological studies
                                         7440-50-8D, Copper, radionuclides,
                          7440-65-5D, Yttrium, radionuclides, biological
     biological studies
               7440-69-9D, Bismuth, radionuclides, biological studies
     studies
     7440-74-6D, Indium, radionuclides, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (cyclic amines binding to, as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     15715-08-9, Iodine-123, biological studies
                                                 15750-15-9, Indium-111,
     biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for gamma ray
        imaging; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     13981-56-1, Fluorine-18, biological studies
                                                 14158-30-6, Iodine-124,
     biological studies
                        14809-47-3, Bromine-75, biological studies
     15765-38-5, Bromine-76, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for positron imaging;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     10043-66-0, Iodine-131, biological studies
                                                 10098-91-6, Yttrium-90,
     biological studies
                         14265-75-9, Lutetium-177, biological studies
     14378-26-8, Rhenium-188, biological studies
                                                  14913-49-6, Bismuth-212,
     biological studies
                         14998-63-1, Rhenium-186, biological studies
     15623-45-7, Radium-223, biological studies
                                                15755-39-2, Astatine-211,
     biological studies
                        15757-86-5, Copper-67, biological studies
     15776-20-2, Bismuth-213, biological studies 29687-57-8, Samarium-157,
    biological studies
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RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for radiotherapy;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     9013-20-1D, Streptavidin, immobilized
     RL: BUU (Biological use, unclassified); DEV (Device component use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (extracorporeal adsorption device contg., in kit for removal
        of nontargeted biomol. conjugate from blood circulation; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
IT
     14133-76-7, Technetium-99, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (metastable, effector agent contg., in trifunctional reagent, for gamma
        ray imaging; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
IT
     13981-55-0, Indium-114, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (metastable, effector agent contg., in trifunctional reagent, for
        radiotherapy; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     60-00-4D, EDTA, derivs.
                               67-43-6D, DTPA, derivs.
                                                         3565-84-2
     56491-86-2, NOTA
                       60239-18-1, DOTA 60239-22-7, TETA
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     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (radionuclide-binding, as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     9013-20-1, Streptavidin
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (trifunctional reagent contg. affinity ligand binding to; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
ΙT
     58-85-5D, Biotin, conjugates with crosslinking agent binding to effect
     agent and to biomol. reactive moiety 99-31-0D,
     3,5-Dicarboxyaniline, conjugates with affinity ligand and effector agent
     and biomol. reactive moiety 108-72-5D, 1,3,5-Triaminobenzene, conjugates
     with affinity ligand and effector agent and biomol. reactive moiety
     533-48-2D, Desthiobiotin, conjugates with crosslinking agent binding to
     effect agent and to biomol. reactive moiety 535-87-5D,
     3,5-Diaminobenzoic acid, conjugates with affinity ligand and effector
     agent and biomol. reactive moiety 554-95-0D, 1,3,5-Tricarboxybenzene,
     conjugates with affinity ligand and effector agent and biomol. reactive
    moiety
             669-72-7D, Norbiotin, conjugates with crosslinking agent binding
     to effect agent and to biomol. reactive moiety
                                                    1784-22-1D, Homobiotin,
     conjugates with crosslinking agent binding to effect agent and to biomol.
     reactive moiety
                      3376-83-8D, Biotin sulfoxide, conjugates with
     crosslinking agent binding to effect agent and to biomol. reactive moiety
     13395-35-2D, Iminobiotin, conjugates with crosslinking agent binding to
    effect agent and to biomol. reactive moiety 14474-91-0D, Oxybiotin,
     conjugates with crosslinking agent binding to effect agent and to biomol.
     reactive moiety
                      22342-46-7D, Diaminobiotin, conjugates with crosslinking
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agent binding to effect agent and to biomol. reactive moiety
     40720-05-6D, Biotin sulfone, conjugates with crosslinking agent binding to
     effect agent and to biomol. reactive moiety 254441-23-1
                                                                   254441-24-2D,
                             254441-26-4
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     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
RE.CNT
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     Trifunctional reagent for conjugation to a biomolecule for use in
     diagnosis and therapy
     Wilbur, D. Scott; Sandberg, Bengt E. B.
    Department of Radiation Oncology, University of Washington, USA; Mitra
    Medical Technology AB
    PCT Int. Appl., 41 pp.
    CODEN: PIXXD2
    Patent
    English
    ICM G01N033-543
     ICS C07K019-00; A61K039-395; A61K047-48; A61K051-00; A61K049-00
     9-15 (Biochemical Methods)
     Section cross-reference(s): 1, 8, 15, 63
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AΒ
     A reagent for conjugation to a biomol. for diagnosis and treatment of
     human and animal conditions and diseases is described, wherein the reagent
     is a single mol. with at least three functional parts and a) wherein a
     trifunctional crosslinking moiety is coupled to b) an affinity ligand via
     a linker 1, said affinity ligand being capable of binding with another
     mol. having affinity for said liquid; to c) an effector agent, optionally
     via a linker 2, said effector agent exerting its effects on cells, tissues
     and/or humorous mols. in vivo or ex vivo; and to d) a biomol. reactive
     moiety, optionally via a linker 3, said moiety being capable of forming a
     bond between the reagent and the biomol. The affinity ligand is esp.
     biotin or a biotin deriv. The effector agent is a toxin, an enzyme
     capable of converting a prodrug to an active drug, an immunosuppressant,
     an immunostimulant, or a radionuclide-binding agent, with or without the
     radionuclide.
ST
     trifunctional reagent biomol conjugation diagnosis therapy; biotin
     trifunctional reagent biomol conjugate diagnosis therapy; toxin
     trifunctional reagent biomol conjugate therapy; prodrug converting enzyme
     trifunctional reagent conjugate; immunomodulator trifunctional reagent
     conjugate; radiotherapy trifunctional reagent conjugate; imaging agent
     trifunctional reagent conjugate
ΙT
     Proteins, specific or class
     RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (affinity ligand-binding, for removal of nontargeted biomol. conjugate
        from blood circulation; trifunctional reagent for conjugation to a
        biomol. for use in diagnosis and therapy)
IT
     Ligands
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical
     study); BIOL (Biological study); PROC (Process); USES (Uses)
        (affinity, trifunctional reagent contg.; trifunctional reagent for
        conjugation to a biomol. for use in diagnosis and therapy)
ΙT
     Functional groups
        (ammonio group, linkers contg.; trifunctional reagent for conjugation
        to a biomol. for use in diagnosis and therapy)
IT
     Separators
        (blood plasma, in kit for removal of nontargeted biomol. conjugate from
        blood circulation; trifunctional reagent for conjugation to a biomol.
        for use in diagnosis and therapy)
IT
    Amines, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (cyclic, radionuclide-binding, as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
    Lung, disease
```

```
(embolism; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
ΙT
     Carboxylic acids, properties
     RL: PRP (Properties)
        (esters, linkers contg.; trifunctional reagent for conjugation to a
        biomol. for use in diagnosis and therapy)
IT
     Adsorption apparatus
        (extracorporeal, in kit for removal of nontargeted biomol.
        conjugate from blood circulation; trifunctional reagent for conjugation
        to a biomol. for use in diagnosis and therapy)
IT
        (extracorporeal, nontargeted biomol. conjugate removal from;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Affinity chromatographic stationary phases
        (for removal of nontargeted biomol. conjugate from blood circulation;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
IT
     Imaging
        (gamma-ray; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
     Vinyl compounds, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (halo, halogen radionuclide-contg., as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Aryl halides
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (halogen radionuclide-contg., as effector agent in trifunctional
        reagent; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
TΨ
     Avidins
     Receptors
     RL: BUU (Biological use, unclassified); DEV (Device component use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (immobilized, extracorporeal adsorption device contq., in kit
        for removal of nontargeted biomol. conjugate from blood circulation;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IΤ
     Heart, disease
        (infarction; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
IT
     Ethers, properties
     Sulfonates
     Thioethers
     RL: PRP (Properties)
        (linkers contg.; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
TТ
     Circulation
        (nontargeted biomol. conjugate removal from; trifunctional reagent for
        conjugation to a biomol. for use in diagnosis and therapy)
ΙT
     Enzymes, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
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(prodrug-metabolizing, trifunctional reagent contg., as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Drug delivery systems
        (prodrugs, trifunctional reagent contg. enzymes metabolizing;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
     Brain, disease
ΤТ
        (stroke; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
     Radiotherapy
        (targeted; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
IT
     Disease, animal
        (treatment of; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     Avidins
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (trifunctional reagent contg. affinity ligand binding to; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
     Body fluid
IT
        (trifunctional reagent contq. effector agent acting on mols. in;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     Animal tissue
     Cell
        (trifunctional reagent contg. effector agent acting on; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
IT
     Radionuclides, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (trifunctional reagent contg. moieties binding to, as effector agent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     Immunostimulants
     Immunosuppressants
        (trifunctional reagent contg., as effector agent; trifunctional reagent
        for conjugation to a biomol. for use in diagnosis and therapy)
IT
     Enzymes, biological studies
     Toxins
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (trifunctional reagent contg., as effector agent; trifunctional reagent
        for conjugation to a biomol. for use in diagnosis and therapy)
IT
     Animal
     Atherosclerosis
     Biochemical molecules
     Diagnosis
     Drug targeting
     Mammal (Mammalia)
     Neoplasm
     Positron-emission tomography
     Therapy
     Vertebrate (Vertebrata)
        (trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IT
    Reagents
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ANST (Analytical study); BIOL (Biological study); RACT (Reactant or
     reagent); USES (Uses)
        (trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IΤ
     Crosslinking agents
        (trifunctional; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
ΙT
     Thrombosis
        (venous, deep; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     9025-15-4, Biotinidase
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (biotin-contg. reagent with stability against cleavage with;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     7439-92-1D, Lead, radionuclides, biological studies
                                                          7439-94-3D.
     Lutetium, radionuclides, biological studies
                                                    7440-19-9D, Samarium,
     radionuclides, biological studies
                                         7440-50-8D, Copper, radionuclides,
    biological studies
                          7440-65-5D, Yttrium, radionuclides, biological
               7440-69-9D, Bismuth, radionuclides, biological studies
     7440-74-6D, Indium, radionuclides, biological studies
    RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (cyclic amines binding to, as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
IT
     15715-08-9, Iodine-123, biological studies 15750-15-9, Indium-111,
    biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for gamma ray
        imaging; trifunctional reagent for conjugation to a biomol. for use in
        diagnosis and therapy)
IΤ
     13981-56-1, Fluorine-18, biological studies
                                                  14158-30-6, Iodine-124,
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                          14809-47-3, Bromine-75, biological studies
    15765-38-5, Bromine-76, biological studies
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     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for positron imaging;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
TΤ
    10043-66-0, Iodine-131, biological studies
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                         188, biological studies 14913-49-6, Bismuth-212, 14998-63-1, Rhenium-186, biological studies
    14378-26-8, Rhenium-188, biological studies
    biological studies
    15623-45-7, Radium-223, biological studies
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                         15757-86-5, Copper-67, biological studies
    15776-20-2, Bismuth-213, biological studies 29687-57-8, Samarium-157,
    biological studies
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     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
    ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (effector agent contg., in trifunctional reagent, for radiotherapy;
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RL: ARG (Analytical reagent use); RCT (Reactant); THU (Therapeutic use);

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trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     9013-20-1D, Streptavidin, immobilized
     RL: BUU (Biological use, unclassified); DEV (Device component use); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (extracorporeal adsorption device contg., in kit for removal
        of nontargeted biomol. conjugate from blood circulation; trifunctional
        reagent for conjugation to a biomol. for use in diagnosis and therapy)
     14133-76-7, Technetium-99, biological studies
ΙT
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     (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use);
     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (metastable, effector agent contg., in trifunctional reagent, for gamma
        ray imaging; trifunctional reagent for conjugation to a biomol. for use
        in diagnosis and therapy)
TΤ
     13981-55-0, Indium-114, biological studies
     RL: ARG (Analytical reagent use); BPR (Biological process); BSU
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     ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT
     (Reactant or reagent); USES (Uses)
        (metastable, effector agent contg., in trifunctional reagent, for
        radiotherapy; trifunctional reagent for conjugation to a biomol. for
        use in diagnosis and therapy)
IT
     60-00-4D, EDTA, derivs.
                               67-43-6D, DTPA, derivs.
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     56491-86-2, NOTA
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        (radionuclide-binding, as effector agent in trifunctional reagent;
        trifunctional reagent for conjugation to a biomol. for use in diagnosis
        and therapy)
ΙT
     9013-20-1, Streptavidin
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (trifunctional reagent contg. affinity ligand binding to; trifunctional
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IT
     58-85-5D, Biotin, conjugates with crosslinking agent binding to effect
    agent and to biomol. reactive moiety 99-31-0D,
     3,5-Dicarboxyaniline, conjugates with affinity ligand and effector agent
    and biomol. reactive moiety 108-72-5D, 1,3,5-Triaminobenzene, conjugates
    with affinity ligand and effector agent and biomol. reactive moiety
     533-48-2D, Desthiobiotin, conjugates with crosslinking agent binding to
     effect agent and to biomol. reactive moiety 535-87-5D,
     3,5-Diaminobenzoic acid, conjugates with affinity ligand and effector
    agent and biomol. reactive moiety 554-95-0D, 1,3,5-Tricarboxybenzene,
    conjugates with affinity ligand and effector agent and biomol. reactive
            669-72-7D, Norbiotin, conjugates with crosslinking agent binding
     to effect agent and to biomol. reactive moiety 1784-22-1D, Homobiotin,
    conjugates with crosslinking agent binding to effect agent and to biomol.
                      3376-83-8D, Biotin sulfoxide, conjugates with
     reactive moiety
    crosslinking agent binding to effect agent and to biomol. reactive moiety
    13395-35-2D, Iminobiotin, conjugates with crosslinking agent binding to
    effect agent and to biomol. reactive moiety
                                                  14474-91-0D, Oxybiotin,
    conjugates with crosslinking agent binding to effect agent and to biomol.
    reactive moiety
                      22342-46-7D, Diaminobiotin, conjugates with crosslinking
    agent binding to effect agent and to biomol. reactive moiety
    40720-05-6D, Biotin sulfone, conjugates with crosslinking agent binding to
    effect agent and to biomol. reactive moiety
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        (trifunctional reagent for conjugation to a biomol. for use in
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RE.CNT
             THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Beckman Instruments Inc; EP 0310361 A2 1989 CAPLUS
(2) Board Of Regents Of The University Of Washington; WO 9729114 A1 1997 CAPLUS
(3) Boehringer Mannheim Gmbh; EP 0618192 A1 1994 CAPLUS
(4) Cancer Research Campaign Technology Limited; WO 8910140 A1 1989 CAPLUS
(5) Gaetjens, E; US 5134071 A 1992 CAPLUS
(6) Hybritech Incorporated; WO 9302105 A1 1993 CAPLUS
(7) Immunomedics Inc; WO 9604313 A1 1996 CAPLUS
(8) Jacobson, K; US 5310916 A 1994 CAPLUS
(9) Muzykantov, V; Proc Natl Acad Sci 1996, V93, P5213 CAPLUS
(10) Otusji, E; 1997, 20, CAPLUS
(11) Otusji, E; Cancer Res 1997, V88(2), P205 CAPLUS
=> d 118 1-4
L18 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
    2002:523951 CAPLUS
    137:228855
    Trifunctional conjugation reagents. Reagents that contain a biotin and a
     radiometal chelation moiety for application to extracorporeal
    affinity adsorption of radiolabeled antibodies
    Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Kegley, Brian B.;
    Nilsson, Rune; Sandberg, Bengt E. B.; Brechbiel, Martin
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
    Bioconjugate Chemistry (2002), 13(5), 1079-1092
    CODEN: BCCHES; ISSN: 1043-1802
    American Chemical Society
    Journal
    English
RE.CNT 62
             THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
L18 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
    2001:923565 CAPLUS
    136:42919
    Biotin derivatives for an extracorporeal device
    Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune
    Mitra Medical Technology AB, Swed.; University of Washington
    PCT Int. Appl., 45 pp.
    CODEN: PIXXD2
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     132:90367
TΙ
     Trifunctional reagent for conjugation to a biomolecule for use in
     diagnosis and therapy
     Wilbur, D. Scott; Sandberg, Bengt E. B.
IN
PA
     Dept. of Radiation Oncology, University of Washington, USA; Mitra Medical
     Technology AB
SO
     PCT Int. Appl., 48 pp.
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ΤI
     Trifunctional reagent for conjugation to a biomolecule for use in
     diagnosis and therapy
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IN
     Wilbur, D. Scott; Sandberg, Bengt E. B.
     Department of Radiation Oncology, University of Washington, USA; Mitra
PA
     Medical Technology AB
SO
     PCT Int. Appl., 41 pp.
     CODEN: PIXXD2
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DL21 IS NOT A RECOGNIZED COMMAND
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L21 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN
     2002:778699 CAPLUS
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     137:299916
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     Peptide-containing compounds for targeting cells expressing NP-1 receptor
IN
     Von Wronski, Mathew A.; Marinelli, Edmund R.; Nunn, Adrian D.; Pillai,
     Radhakrishna; Ramalingam, Kondareddiar; Tweedle, Michael F.; Linder,
     Karen; Nanjappan, Palaniappa; Raju, Natarajan
PA
     USA
SO
     U.S. Pat. Appl. Publ., 85 pp., Cont.-in-part of U.S. Ser. No. 585,364.
     CODEN: USXXCO
ידת
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   US 2002147136
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L21 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS
     2002:534031 CAPLUS
ΑN
DN
     137:93597
     Preparation and use of phenoxyalkylamino-linked dimers as sodium channel
ΤI
IN
    Marquess, Daniel; Choi, Seok-ki; Beattie, David T.; Griffin, John H.;
     Armstrong, Scott; Church, Timothy J.; Jenkins, Thomas E.
PA
     Advanced Medicine, Inc., USA
SO
    U.S., 121 pp., Cont.-in-part of U.S. Ser. No. 325,563, abandoned.
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              THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 59
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L21 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2003 ACS AN 2001:885834 CAPLUS

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DN
     136:25104
TI
     Peptide-containing compounds for targeting endothelial cells, compositions
     containing the same and methods for their use
     Von Wronski, Mathew A.; Marinelli, Edmund R.; Nunn, Adrian D.; Pillai,
ΙN
     Radhakrishna; Ramalingam, Kondareddiar; Tweedle, Michael F.; Linder,
     Karen; Nanjappan, Palaniappa; Raju, Natarajan
PA
     Bracco Research USA, USA
     PCT Int. Appl., 146 pp.
SO
     CODEN: PIXXD2
DT
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LΑ
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PRAI US 2000-585364
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L21 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2003 ACS
     2001:640098 CAPLUS
AN
TI
     Drug delivery and selective targeting by vitamin B12 derivatives
ΑU
     Reinhard, Kathryn S.; Gao, Xiang; Chaung, Danny K.; Wilson, Stephen R.
CS
     Department of Chemistry, New York University, New York, NY, 10003, USA
SO
     Abstracts of Papers, 222nd ACS National Meeting, Chicago, IL, United
     States, August 26-30, 2001 (2001), MEDI-279 Publisher: American Chemical
     Society, Washington, D. C.
     CODEN: 69BUZP
DT
     Conference; Meeting Abstract
LA
     English
L21 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN
     2001:284303 CAPLUS
DN
     135:42876
ΤI
     Peptide and small molecule microarray for high throughput cell adhesion
     and functional assays
     Falsey, James R.; Renil, M.; Park, Steven; Li, Shijun; Lam, Kit S.
ΑU
CS
     UC Davis Cancer Center Division of Hematology/Oncology and Department of
     Internal Medicine, University of California Davis, Sacramento, CA, 95817,
SO
     Bioconjugate Chemistry (2001), 12(3), 346-353
     CODEN: BCCHES; ISSN: 1043-1802
PΒ
     American Chemical Society
DT
     Journal
LΑ
     English
RE.CNT 42
              THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L21 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS
    2001:201927 CAPLUS
AN
ΤI
    Synthesis and evaluation of protein biotinylation reagents that also
     contain UV and/or fluorescence absorbing moieties
```

Wilbur, D. Scott; Chyan, Ming-Kuan; Hamlin, Donald K.; Sandberg, Bengt E.

ΑU

В.

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CS
     Radiation Oncology, University of Washington, Seattle, WA, 98103, USA
SO
     Abstr. Pap. - Am. Chem. Soc. (2001), 221st, MEDI-031
     CODEN: ACSRAL; ISSN: 0065-7727
PB
     American Chemical Society
DT
     Journal; Meeting Abstract
LA
     English
L21 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN
     2000:145059 CAPLUS
DN
     132:191408
ΤI
     Rapid quantitative analysis of proteins or protein function in complex
     mixtures using affinity labeling reagents and mass spectrometry
IN
     Aebersold, Rudolf Hans; Gelb, Michael H.; Gygi, Steven P.; Scott, C.
     Ronald; Turecek, Frantisek; Gerber, Scott A.; Rist, Beate
PA
     University of Washington, USA
SO
     PCT Int. Appl., 116 pp.
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LΑ
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L21 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS
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ΑN
DN
     132:302964
ΤI
     High-Affinity Pentavalent Ligands of Escherichia coli Heat-Labile
     Enterotoxin by Modular Structure-Based Design
ΑU
     Fan, Erkang; Zhang, Zhongsheng; Minke, Wendy E.; Hou, Zheng; Verlinde,
     Christophe L. M. J.; Hol, Wim G. J.
CS
     Department of Biological Structure Biomolecular Structure Center and
     Howard Hughes Medical Institute, University of Washington, Seattle, WA,
     98195, USA
     Journal of the American Chemical Society (2000), 122(11), 2663-2664
SO
     CODEN: JACSAT; ISSN: 0002-7863
PΒ
     American Chemical Society
DT
     Journal
LΑ
     English
RE.CNT 22
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L21 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS
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AN

DN

1999:369591 CAPLUS

131:116513

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ΤI
     Efficient assembly of peptomers on continuous surfaces
AU
     Ast, Thomas; Heine, Niklas; Germeroth, Lothar; Schneider-Mergener, Jens;
     Wenschuh, Holger
CS
     Institut fur Medizinische Immunologie, Universitatsklinikum Charite,
     Humboldt-Universitat zu Berlin, Berlin, 10098, Germany
     Tetrahedron Letters (1999), 40(23), 4317-4318
SO
     CODEN: TELEAY; ISSN: 0040-4039
PB
     Elsevier Science Ltd.
DT
     Journal
LΑ
     English
RE.CNT 9
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L21
     ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN
     1997:708440 CAPLUS
DN
     127:298612
TI
     Biotin Reagents for Antibody Pretargeting. 2. Synthesis and in Vitro
     Evaluation of Biotin Dimers and Trimers for Crosslinking of Streptavidin
ΑU
     Wilbur, D. Scott; Pathare, Pradip M.; Hamlin, Donald K.; Weerawarna, S.
     Department of Radiation Oncology, University of Washington, Seattle, WA,
CS
     98195, USA
SO
     Bioconjugate Chemistry (1997), 8(6), 819-832
     CODEN: BCCHES; ISSN: 1043-1802
     American Chemical Society
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DT
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     ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN
     1997:542454 CAPLUS
DN
     127:220519
ΤI
     Preparation of biotin containing compounds with water soluble
     linker moieties for use as radionuclides and streptavidin
     crosslinking agents
     Wilbur, Scott D.; Pathare, Pradip M.; Weerawarna, S. Ananda; Hamlin,
TN
     Donald K.
PA
     Board of Regents of the University of Washington, USA
SO
     PCT Int. Appl., 80 pp.
     CODEN: PIXXD2
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L21 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2003 ACS
     1997:433652 CAPLUS
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DN 127:121587

TI Biotin reagents for antibody pretargeting. Synthesis, radioiodination and in vitro evaluation of water soluble, biotinidase resistant biotin

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derivatives
ΑU
     Wilbur, D. Scott; Hamlin, Donald K.; Pathare, Pradip M.; Weerawarna, S.
CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
     Bioconjugate Chemistry (1997), 8(4), 572-584
SO
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     Journal
LΑ
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L21
     ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN
     1997:155067 CAPLUS
DN
     126:207193
TΙ
     Synthesis of Cobalamin Dimers Using Isophthalate Crosslinking of Corrin
     Ring Carboxylates and Evaluation of Their Binding to Transcobalamin. 2
     Pathare, Pradip M.; Wilbur, D. Scott; Hamlin, Donald K.; Heusser, Shannon;
ΑU
     Quadros, Edward V.; McLoughlin, Patricia; Morgan, A. Charles
CS
     Department of Radiation Oncology, University of Washington, Seattle, WA,
     98195, USA
     Bioconjugate Chemistry (1997), 8(2), 161-172
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PΒ
     American Chemical Society
DT
     Journal
LΑ
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